Early colorectal cancer from “de novo” carcinogenesis with submucosal invasion: a case report and review of the literature

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Abstract

Background: Colorectal cancer (CRC) mostly develops through the traditional “adenoma-carcinoma sequence”, however there is a rare “de novo” carcinogenic pathway in which cancer originates from normal mucosa. Here, we report a case of early CRC caused by “de novo” carcinogenesis with submucosal invasion and conduct a literature review of this special type of CRC.

Case presentation: A 66-year-old man underwent a screening colonoscopy that revealed a polyp-like lesion (type 0-IIa+IIc in the Paris classification) approximately 0.5 cm in diameter in the descending colon. The patient underwent endoscopic submucosal dissection (ESD); postoperatively, he was pathologically diagnosed with moderately differentiated adenocarcinoma without an adenomatous component from the “de novo” carcinogenic pathway, accompanied by submucosal invasion to a depth of 600 µm. There was no venous or lymphatic permeation, and the margins were negative. A year later, follow-up examinations did not reveal tumour recurrence.

Conclusions: Early “de novo” cancer has a low incidence and a low discovery rate through endoscopy. In this case report, we provide informative details about the presentation of such cancers under endoscopy and further support for the aggressive malignant potential of early “de novo” cancer. The development of advanced CRC can be effectively prevented, and the prognosis of these patients can be improved with active early treatment.

Background

According to the global tumour epidemiology statistics (GLOBOCAN 2020) released by the International Agency for Research on Cancer (IARC) of the World Health Organization, globally, colorectal cancer (CRC) ranked third and second among all malignant tumours in number of new cases and related deaths in 2020, respectively[1]. The development of advanced CRC can be effectively prevented, and the prognosis of these patients can be improved by early diagnosis and treatment.

Nearly 95% of colorectal adenomas lead to CRC through the “adenoma-carcinoma sequence (ACS)” carcinogenic pathway[2, 3]. However, there have been a few cases of CRC developing through a rare “de novo” carcinogenic pathway, showing features of early submucosal infiltration and lymph node metastasis[4, 5]. We report a rare case of early CRC with submucosal invasion caused by “de novo” carcinogenesis and conduct a literature review.

Case Presentation

A 66-year-old male underwent a screening colonoscopy 1 year ago in our outpatient department. He had no history of chronic diseases or family history of genetic diseases. Colonoscopy showed a polyp-like lesion (type 0-IIa + IIc in the Paris classification) approximately 0.5 cm in diameter in the descending colon. Narrow-band imaging (NBI) showed a brownish colour that was star-shaped in the concave area and spiny-shaped at the border (Fig. 1a, b). The endoscopic features of this lesion were empirically

different from those of common colorectal adenomas, so we performed two tissue biopsies. Pathological examination of the biopsied samples revealed moderately differentiated adenocarcinoma (Fig. 2a, b).

We communicated with the patient that additional assessments were recommended to assess the depth of tumour invasion, including laparoscopic surgery or minimally invasive endoscopic surgery, with the patient choosing the latter option. Preoperatively, the routine blood tests, cardiopulmonary function tests and enhanced abdominal computed tomography (CT) examinations were unremarkable, and there were no obvious abnormalities. Magnifying endoscopy (ME) was performed preoperatively and showed that there was a shallow scar at the site of the lesion with normal epithelial repair in the biopsy area, while repaired spindle-shaped vessels and a type I pattern of approximately round pits could be seen at the gland duct opening (Fig. 3a, b).

The patient underwent an additional endoscopic submucosal dissection (ESD) operation two weeks later, with no related surgical complications (Fig. 4a ~ f). After ESD, the pathological diagnosis was moderately differentiated adenocarcinoma measuring 0.2*0.2 cm in size without an adenomatous component and submucosal invasion to a depth of 600 µm; there was no venous or lymphatic permeation, and the margins were negative (Fig. 5a ~ d). The patient was then discharged from the hospital. One year later, follow-up examinations did not reveal tumour recurrence.

Discussion

CRC is one of the most common gastrointestinal tumours and is diagnosed directly by colonoscopy. The classic carcinogenic pathway, ACS, has been widely accepted, while the “de novo” carcinogenic pathway is rarely reported[6]. “De novo” cancer is a special colorectal adenocarcinoma without an adenomatous component that directly develops from the normal mucosal epithelium[7]. As early as the 1980s, Japanese scholars reported that they found 3 cases of minute early cancers (3–5 mm in diameter) in the postoperative background mucosa of 18 cases of CRCs, and these were diagnosed as “de novo” cancers[8]. Because of their low incidence and low discovery rate through endoscopy, “de novo” cancer is rarely described in case reports (Table 1).

Table 1
Summary patients with “de novo” cancer in the case report literature

Author(year)	Sex	Age	Endoscopic features	Infiltration and metastasis	Treatment	Prognosis
Naoyuki et al.(2001)[9]	M	70	Type* 0-Ilc, 2 cm in diameter, in the transverse colon	No mention	No treatment	Advanced carcinoma 15 months later
Takeshi et al.(2007) [10]	M	47	Type* 0-IIa + Ilc, 5 mm in diameter, in the sigmoid colon	Submucosal invasion and Intermediate lymph node metastasis	laparoscopic-assisted sigmoidectomy	No recurrence 1 year later
Minori et al. (2011)[11]	F	35	Type* 0-Is + Ilc, 12 mm in diameter, in the transverse colon	Submucosal invasion and systemic metastasis	EMR [□]	No mention
Yoshihiro et al.(2016) [12]	F	75	Type* 0-IIa, 3 mm in diameter, in the sigmoid colon	Intramucosal	EMR [□]	No mention
* Type, in the Paris classification[13]						
□ EMR, endoscopic mucosal resection						

Early research on “de novo” cancer mainly comes from Japanese scholars. The characteristics of “de novo” cancer in the early stage include a superficial depressed lesion, a diminutive size with a diameter smaller than 1 cm, early submucosal invasion and distant metastasis[14, 15]. Some scholars believe that the adenoma component may be destroyed by adenocarcinoma during tumour progression. Ex-adenocarcinoma is considered a “de novo” cancer. However, early “de novo” tumours smaller than 1 cm are unlikely to be destroyed[16–17]. The case we reported meets the above clinical features.

Kudo[18–19] found some early CRCs with semi-depressed and semi-elevated morphology. The pathology of the mainly depressed area hints that adenocarcinoma appears in the mucosal layer, while the peripheral elevated area has invaded the submucosa. Takeshi et al[10] reported a case of a type 0-IIa + Ilc

tumour with submucosal invasion and intermediate lymph node metastasis, while Minori et al[11] reported a case of a type 0-Is + IIc tumour with submucosal invasion and systemic metastasis. With the development of submucosal invasion and metastasis, the morphology of “de novo” cancer may evolve from type 0-IIc to type 0-IIa + IIc or type 0-Is + IIc. Therefore, it is suggested that the polyp-like morphology in this case is caused by submucosal invasion of the “de novo” cancer. This tumour was easily misdiagnosed by us as an adenomatous polyp.

Typically, NBI ME is used to evaluate the invasive depth of early CRC, which is diagnosed by the type of pit pattern[20]. Type IIIs pit patterns mostly exist in superficial depressed-type lesions, while type V pit patterns often suggest submucosal invasion. No additional data have reported on the detailed features of “de novo” cancer under NBI ME. A limitation of this case is that normal epithelial repair after biopsy affects the observation of pit patterns for diagnosis by NBI ME.

Surgery is recommended for early stage “de novo” cancer because of its aggressive malignant potential. Both Takeshi et al[10] and Minori et al[11] reported cases featuring submucosal invasion and metastasis. Takahisa et al[21] also reported that tumour size does not affect the malignancy grade of early invasive CRC. In this report, postoperative pathology revealed submucosal invasion to a depth of 600 µm, which implies a low risk of lymph node metastasis according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines[22]. Although the tumour invaded the submucosa, curative resection by endoscopy was still possible. Diagnostic ESD is feasible if the patient consents to the procedure.

The “de novo” carcinogenic pathway plays an important role in colorectal adenocarcinoma. To reduce missed and misdiagnosed lesions, endoscopists need to recognize “de novo” cancer. In addition, the mechanism and influencing factors of early submucosal invasion and lymph node metastasis need to be further explored.

Conclusion

CRC developing through the “de novo” carcinogenic pathway is rare. The characteristics of “de novo” cancer include a superficial depressed morphology, a diminutive size and aggressive malignant potential in the early stage. Early endoscopic diagnosis and treatment can effectively improve the prognosis of the disease.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of The First Affiliated Hospital of Wannan Medical College.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Availability of data and materials

All data and material are fully available without restriction.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

The first author: Hua Jiang, collected the data, performed a literature review, and produced the draft manuscript. The corresponding author: Chiyi He, conceived and designed the study and edited the final manuscript. All authors read and approved the final manuscript.

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None.

Abbreviations

CRC

Colorectal cancer; ESD: endoscopic submucosal dissection; ACS: adenoma carcinoma sequence; NBI: Narrow-band imaging; ME: magnifying endoscopy; EMR: endoscopic mucosal resection.

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Figures

Figure 1

Endoscopic finding of the lesion. A.White light imaging(WLI). B.Narrow-band imaging(NBI).

Figure 2

The pathology of biopsied samples. A.Hematein-eosin staining,×10. B. Hematein-eosin staining,×40.

Figure 3

The magnifying endoscopy (ME) before operation. A. ME with NBI. B. ME with chromoendoscopy.

Figure 4

The procedure of ESD operation. A. Marking. B. Submucosal injection. C. Edge cutting. D. Submucosal peeling. E. Postoperative wound. F. Postoperative specimen.

Figure 5

The pathology of ESD specimen. A.Hematein-eosin staining, $\times 10$. B.Hematein-eosin staining, $\times 40$. C.Hematein-eosin staining, $\times 100$. D.Desmin staining $\times 40$.