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Early Squamous Cell Carcinoma of the Anal Canal Resected by Endoscopic Submucosal Dissection

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Key Words

Squamous cell carcinoma · Anal canal · Endoscopic submucosal dissection

Abstract

The standard treatment approach for squamous cell carcinoma (SCC) of the anal canal includes abdominoperineal resection and chemoradiotherapy. However, there are currently very few reports of early SCC of the anal canal resected by endoscopic submucosal dissection (ESD). We report 2 rare cases of SCC of the anal canal resected by ESD. In case 1, a 66-year-old woman underwent a colonoscopy due to blood in her stool, and an elevated lesion, 15 mm in size, was identified from the rectum to the dentate line of the anal canal on internal hemorrhoids. The lesion was diagnosed as an early SCC of the anal canal, and ESD was successfully performed. The histopathological diagnosis was SCC in situ. In case 2, a 71-year-old woman underwent a colonoscopy due to constipation, and an elevated lesion, 25 mm in size, was identified from the dentate line to the anal canal. The lesion was diagnosed as early-stage SCC of the anal canal, and ESD was successfully performed. The histopathological diagnosis was SCC in situ. No complications or recurrence after ESD occurred in either case.

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Introduction

Squamous cell carcinoma (SCC) of the anal canal is a relatively rare malignancy, accounting for only approximately 2% of all gastrointestinal carcinomas [1]. The 5-year survival of

patients with SCC of the anal canal has been reported as 58%. There are some reports regarding the potential prognostic factors of this tumor [2]. Similar to other malignant tumors, disease progression has been demonstrated to represent one of the major adverse prognostic factors for SCC of the anal canal [3]. Previously, abdominoperineal resection was the most commonly used treatment procedure for this malignancy; however, SCC has a good sensitivity to chemoradiotherapy and, for this reason, it has become the standard treatment strategy for SCC of the anal canal [4, 5]. On the other hand, there are currently very few reports of early SCC of the anal canal resected by endoscopic submucosal dissection (ESD). Herein, we present 2 rare cases of early SCC of the anal canal resected using this approach.

Case Reports

Case 1

A 66-year-old woman consulted our hospital complaining of blood in her stool. She consequently underwent a colonoscopy. A white, flat, elevated lesion, 15 mm in size, was identified from the rectum to the dentate line of the anal canal on internal hemorrhoids (fig. 1a). Magnifying endoscopy with narrow-band imaging (NBI) showed irregular vascular patterns (dilatation, tortuous running, caliber changes, and different shapes) (fig. 1b). A chromoendoscopy with indigo-carmin dye showed the edge of the lesion clearly; it revealed a lobulated, flat, and elevated lesion (fig. 1c). Next, the lesion was further confirmed using iodine staining (fig. 1d). Endoscopically, it was diagnosed as an early SCC of the anal canal (carcinoma in situ). Subsequently, ESD was performed en bloc without any complications (fig. 1e, f). The resected tumor comprised well-differentiated SCC. Both the vertical and horizontal cut ends of the tumor were negative. In the superficial layer, koilocytosis, a change of cytoplasm with vacuoles, was recognized (fig. 1g). An immunohistochemical evaluation showed strong expressions of p53, Ki-67, and p16, indicating that the patient was likely infected with the human papillomavirus (HPV) (fig. 1h–j). The histopathological diagnosis was SCC in situ without vessel invasion. At the latest follow-up (12 months after ESD), the patient was recurrence-free.

Case 2

A 71-year-old woman consulted our hospital complaining of constipation. She underwent a colonoscopy, and a white, papillary, flat, elevated lesion, 25 mm in size, was identified from the dentate line to the anal canal (fig. 2a). A magnifying endoscopy with NBI showed irregular vascular patterns (dilatation, tortuous running, caliber changes, and different shapes) (fig. 2b). Chromoendoscopy with indigo-carmin dye showed the edge of the lesion clearly and revealed a lobulated, elevated lesion. In addition, this lesion was clearly visible inside the dentate line (fig. 2c) and easily identified by chromoendoscopy with iodine staining (fig. 2d). Subsequently, ESD was performed without any complications. The lesion was resected en bloc with the entire circumference of the rectum lumen (fig. 2e, f); it was found to be composed of SCC. Both the vertical and horizontal cut ends of the tumor were negative. The histopathological diagnosis was SCC in situ without vessel invasion. In the superficial layer, koilocytosis was observed (fig. 2g). An immunohistochemical evaluation showed strong expressions of p53, Ki-67, and p16 (fig. 2h–j). At the latest follow-up (19 months after ESD), she showed no sign of recurrence.

Discussion

SCC of the anal canal is a relatively rare malignancy. It is strongly associated with HPV infection, which is the causative agent in approximately 80–85% of all patients. Anal intercourse and a high lifetime number of sexual partners increase the risk of persistent HPV infection in both men and women, which in turn may eventually lead to malignancy [6]. Among more than 130 different HPV subtypes, HPV16 is the most prevalent in anal carcinoma and is present in up to 89% of all HPV-positive anal carcinoma patients [7–9]. Increased p16 expression is a well-established surrogate marker for tumors with transcriptional active HPV [10]. Moreover, a long-recognized pathognomonic feature of HPV infection is the appearance of halo or koilocytotic cells in the differentiated layers of the squamous epithelium. These koilocytes are squamous epithelial cells that contain an acentric, hyperchromatic nucleus that is displaced by a large perinuclear vacuole [11]. For detecting early SCC of the anal canal, the use of magnifying endoscopy with NBI and indigo-carmin dye spraying has been previously reported [3]. NBI is a novel noninvasive optical technique that uses reflected light to visualize the organ surface and it can be used to qualitatively diagnose and differentiate between neoplastic and nonneoplastic esophageal lesions [12]. Many studies have demonstrated the usefulness of NBI findings by discovering brownish dots [dilated intraepithelial papillary capillary loops (IPCLs)], tortuous IPCLs, caliber changes in IPCLs, a variety in IPCL shapes, demarcation lines, and brownish epithelium in the diagnosis of squamous mucosal high-grade neoplasia [12]. Similarly to esophageal neoplasia, SCC of the anal canal also consists of malignant squamous cells. Therefore, it is considered possible to qualitatively diagnose SCC of the anal canal using NBI. Colorectal ESD has become a standard therapy for large early colorectal carcinomas in Japan [13], largely owing to the fact that it can be used to resect most types of lesions, regardless of their size or location [14]. However, colorectal ESD is more technically demanding than esophageal and gastric ESD, as the anatomic features of the large intestine, which is a long luminal organ with many folds and flexures, hinder the manipulation of the endoscope for some lesions, and due to the fact that the intestinal wall is thin and easy to perforate. There have been some reports indicating that the establishment of a systematic training program for the technically more difficult colorectal ESD, in addition to the further development and refinement of ESD-related instruments, devices, equipment, and injection solutions, may help facilitate the increased use of colorectal ESD throughout the world [14, 15]. We have previously reported on the clinical usefulness of ESD for lesions close to the dentate line, which should be performed with the following considerations in mind: (1) local anesthesia to prevent anal pain should be administered before submucosal injection of hyaluronic acid; (2) a shallow peripheral mucosal incision should be made to prevent bleeding, and (3) the blood vessels should be appropriately handled using hemostatic forceps [15]. As demonstrated in the present study, even in cases of anal canal tumors, we could perform ESD successfully using this procedure. In the future, as the clinicopathologic characteristics and prognosis of early SCC of the anal canal are currently not clear, further studies are needed in order to reveal the indications of ESD for early SCC of the anal canal.

Disclosure Statement

The authors declare that they have no conflicts of interest concerning this paper.

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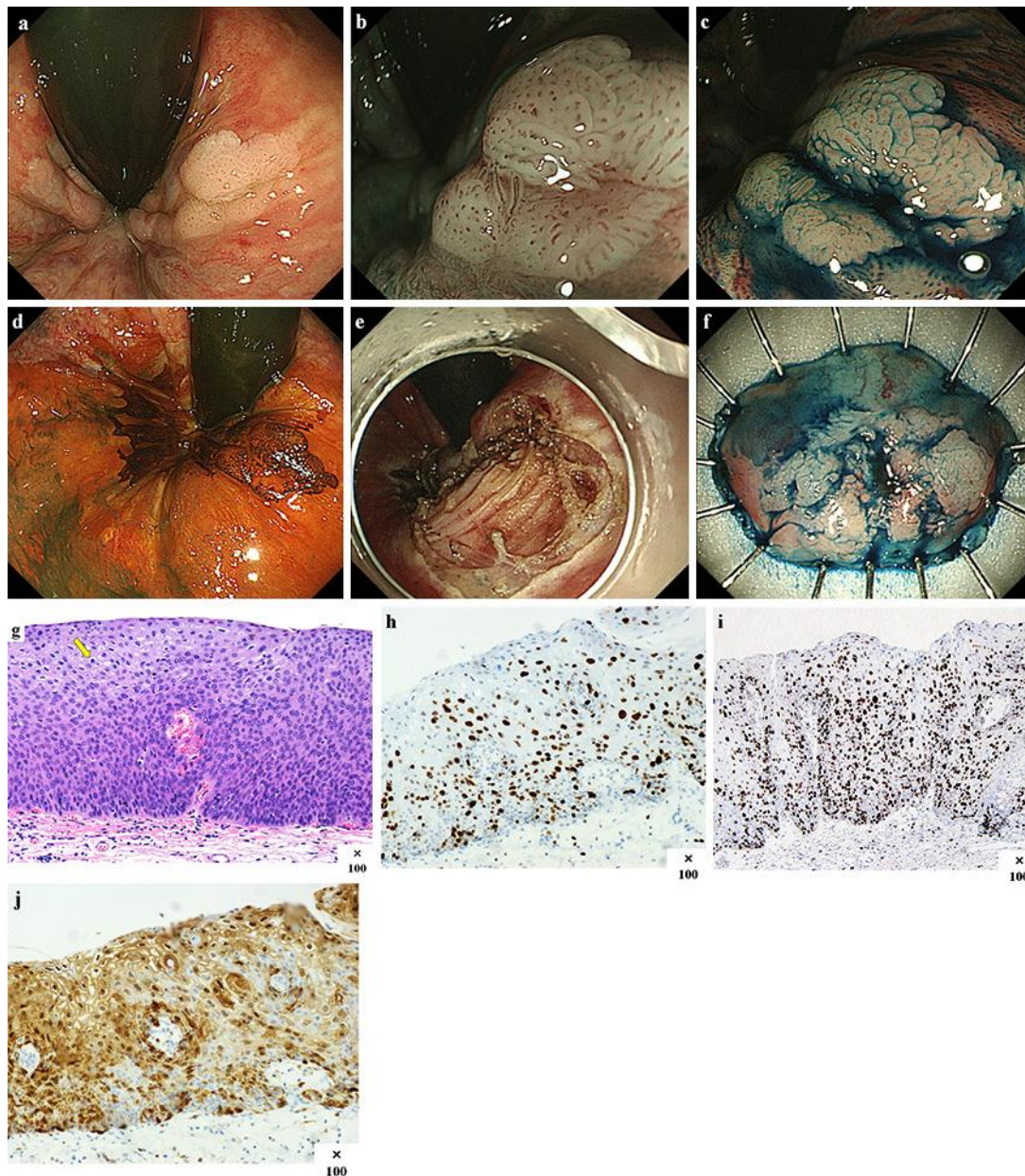


Fig. 1. **a** A white, flat, elevated lesion, 15 mm in size, was identified from the rectum to the dentate line of the anal canal on internal hemorrhoids. **b** NBI showed irregular vascular patterns (dilatation, tortuous running, caliber changes, and different shapes). **c** A chromoendoscopy with indigo-carmin dye showed the edge of the lesion clearly and revealed a lobulated, flat, elevated lesion. **d** The lesion was identified by chromoendoscopy with iodine staining as the stained area, with some unstained parts observed. **e** The ulcer after en bloc resection. **f** The resected specimen. **g** The tumor was composed of well-differentiated SCC in situ. The vertical and horizontal cut ends of the tumor were both negative. In the superficial layer, koilocytosis was recognized. **h–j** An immunohistochemical evaluation showed strong expressions of p53 (**h**), Ki-67 (**i**), and p16 (**j**), indicating that the patient was infected with HPV.

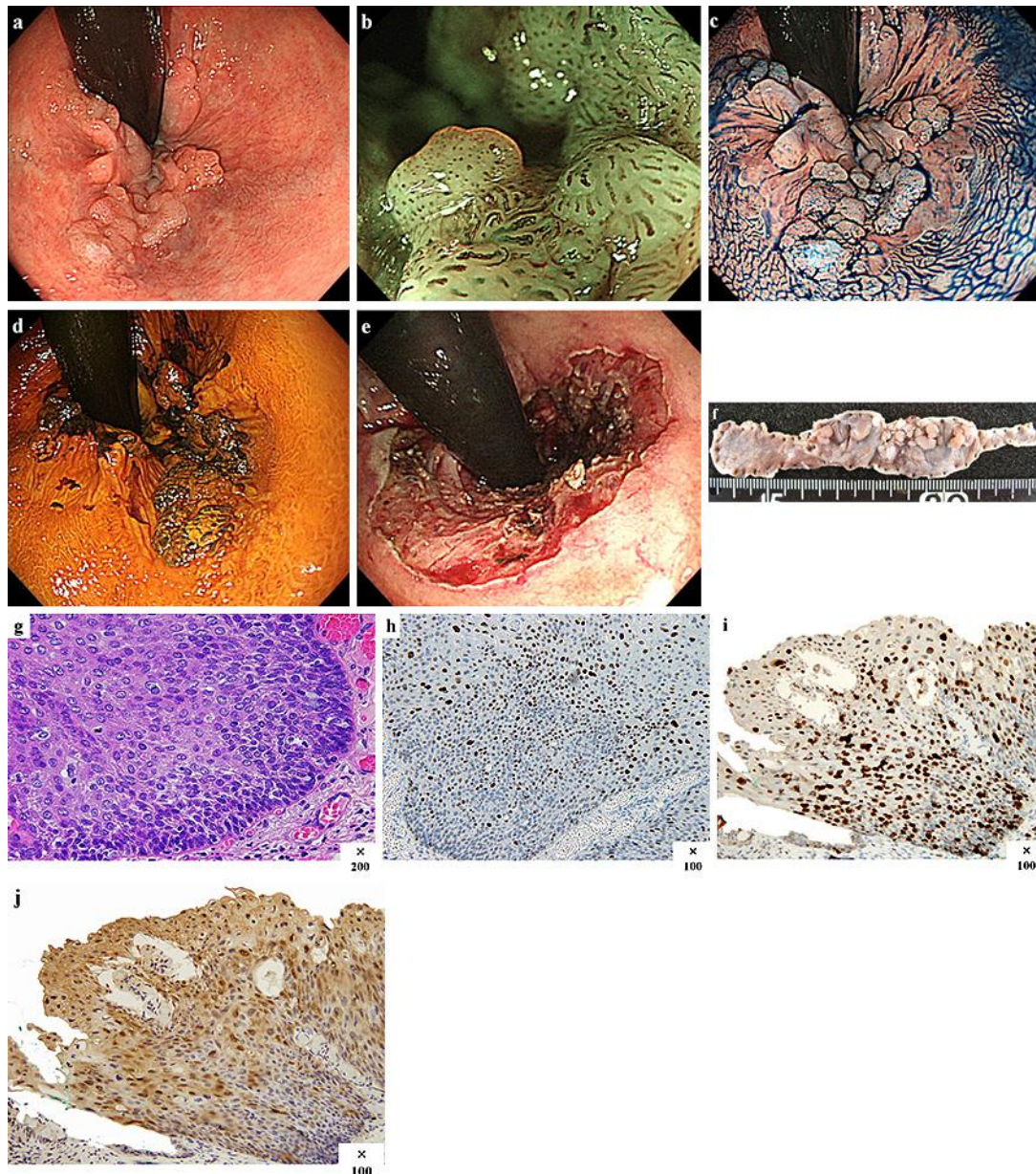


Fig. 2. **a** A white, papillary, flat, elevated lesion, 25 mm in size, was identified from the dentate line to the anal canal. **b** NBI showed irregular vascular patterns (dilatation, tortuous running, caliber changes, and different shapes) at the elevated lesion. **c** A chromoendoscopy with indigo-carmin dye showed the edge of the lesion clearly and revealed a lobulated, elevated lesion. In addition, this lesion was clearly visible inside the dentate line. **d** The lesion was identified by chromoendoscopy with iodine staining as the stained area. **e** The rectal area after en bloc resection showing the entire circumferential ulcer. **f** Macroscopic findings from the resected specimen. **g** The tumor was composed of SCC in situ. The vertical and horizontal cut ends of the tumor were both negative. The histopathological diagnosis was of SCC in situ without vessel invasion. **h–j** An immunohistochemical evaluation showed strong expressions of p53 (**h**), Ki-67 (**i**), and p16 (**j**).