

Endoscopic submucosal dissection for early squamous cell carcinoma in the anal canal and Lugol chromoendoscopy for assessment of the lateral margin



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ABSTRACT

A 66-year-old man underwent follow-up colonoscopy after colon polypectomy. The retroflexed view of the anal canal with white-light imaging revealed a whitish, slightly elevated lesion on the dentate line and an ill-defined flat lesion. A biopsy of the whitish elevation revealed squamous cell carcinoma (SCC), and endoscopic submucosal dissection (ESD) was planned. The lateral margin of the SCC was identified by spraying with Lugol's iodine, and the tumor was resected en bloc with no complications. The pathological findings were SCC in situ with parakeratosis in the whitish elevation and high-grade intraepithelial neoplasia in the ill-defined flat lesion, which exhibited a wide iodine-unstained area by chromoendoscopy. Early SCC in the anal canal is a rare gastrointestinal cancer, and Lugol chromoendoscopy helped visualize the tumor margin for ESD.

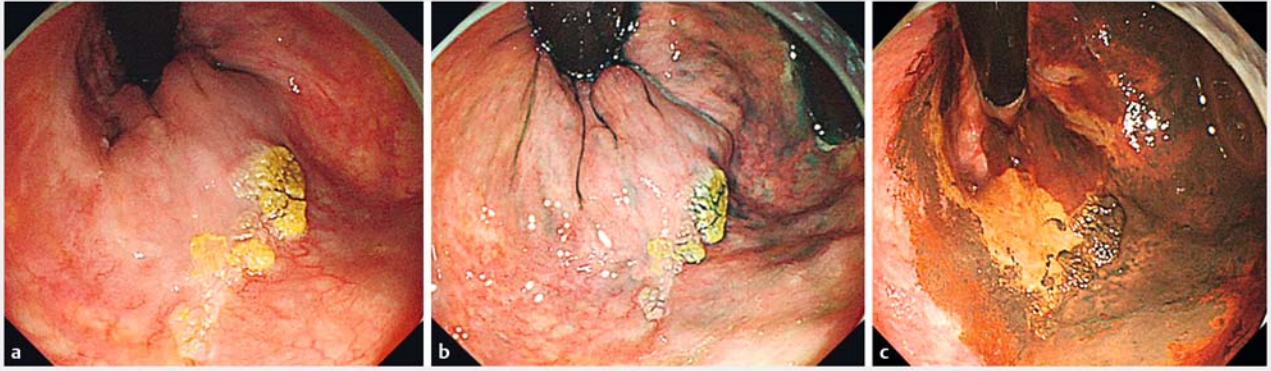
Introduction

Anal canal cancer constitutes approximately 1% of all gastrointestinal cancers, and the incidence rate of squamous cell carcinoma (SCC) in the anal canal has been increasing [1]. In recent years, early diagnosis of SCC in the anal canal has been increasing owing to advances in endoscopic equipment. However, few such cases involving endoscopic submucosal dissection (ESD) have been reported. ESD is a minimally invasive treatment for colorectal tumors without a risk of lymph node metastasis. Accurate evaluation of the extent of the tumor margin when performing ESD is important to prevent local recurrence. Iodine staining facilitates detection of superficial esophageal SCC and dysplasia because mature squamous epithelial cells contain glycogen, which is stained brown by iodine. When the normal maturation of the epithelium is disturbed by dysplasia or neoplasia, the glycogen content is decreased and the lesion remains

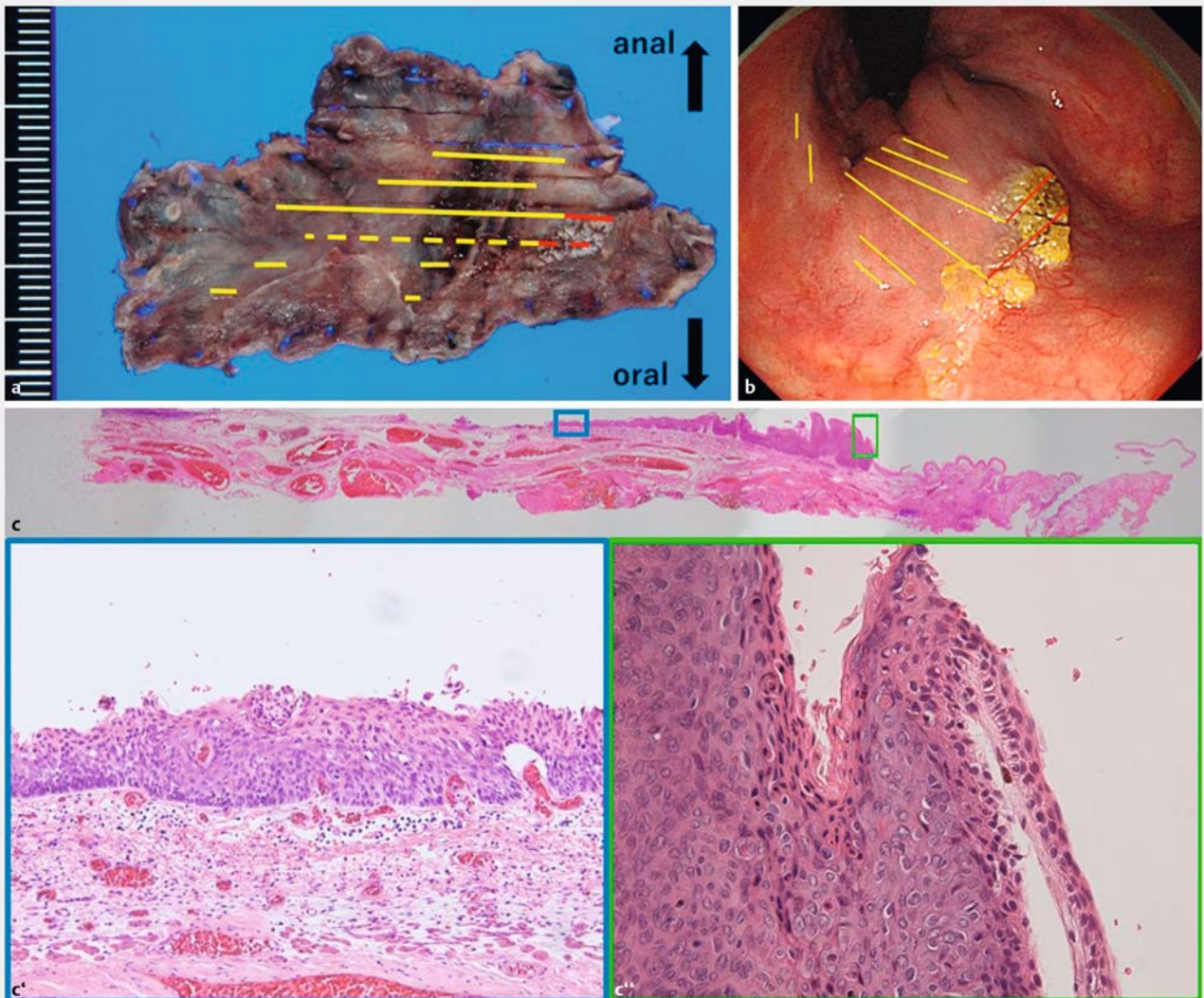
unstained. We herein report a case of early SCC in the anal canal treated by ESD, wherein Lugol chromoendoscopy was performed preoperatively to accurately assess the lateral tumor margin.

Case report

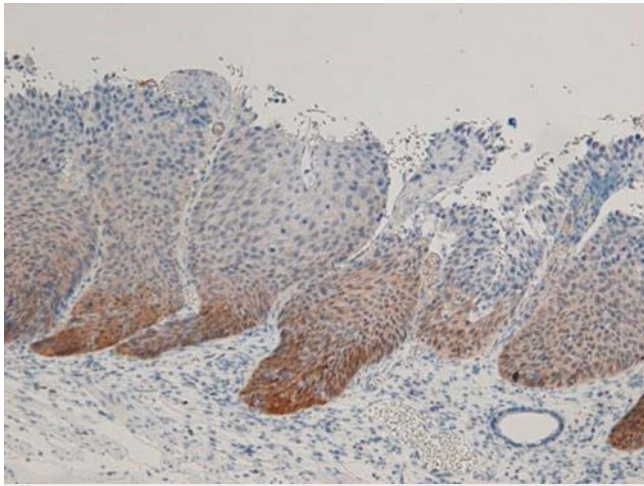
A 66-year-old man underwent follow-up colonoscopy after colon polypectomy. A retroflex view of the anal canal with white-light imaging (WLI) revealed a whitish, slightly elevated lesion of approximately 12 mm in size on the dentate line and an ill-defined flat lesion extending from the dentate line to the anal canal (► Fig. 1a). The extent of the flat lesion was unclear on chromoendoscopy with indigo carmine dye (► Fig. 1b) but was clearly visualized with iodine staining via Lugol chromoendoscopy. It was approximately 25 mm in size (► Fig. 1c). A biopsy of the whitish, slightly elevated lesion revealed SCC. The lesion



► **Fig. 1** **a** Whitish, slightly elevated lesion in association with a flat lesion detected with WLI. The margin of the flat lesion was unclear. **b** Indigo carmine dye was not useful for evaluation of the margin of the ill-defined flat lesion **c** The margin of the ill-defined flat lesion was clearly distinguished with Lugol chromoendoscopy.



► **Fig. 2** **a** The resected specimen (56×35 mm). The red lines indicate the area of SCC in situ. The yellow lines indicate the area of intraepithelial neoplasia. **b** Mapping of the retroflexed view of the anal canal. **c** The specimen is shown within the dotted line. Moderate atypia was present (blue box). Parakeratosis was observed in the superficial layer of the whitish, slightly elevated lesion (green box).



► **Fig. 3** p16 immunostaining of the basal layer of the tumor was positive.

appeared to be shallow on endoscopy, and computed tomography revealed no enlarged lymph nodes or distant metastasis. ESD was performed to resect the tumor en bloc. A pathological examination showed that the whitish elevated lesion was SCC in situ with parakeratosis and that the ill-defined flat lesion was high-grade intraepithelial neoplasia (► **Fig. 2a, b, c', and c''**). The horizontal and vertical margins were free of tumor, and there was no lymphovascular invasion. p16 immunohistochemical staining was positive (► **Fig. 3**), and polymerase chain reaction revealed infection by human papilloma virus 16. The patient was discharged 9 d after the ESD. Computed tomography at 5-mo follow-up revealed no recurrence.

Discussion

Despite an increase in SCCs detected in the anal canal resulting from advances in endoscopic equipment and the diagnostic skill of endoscopists, SCC in situ in the anal canal is still rare.

The prognosis is related to the size of the tumor and the presence of lymph node metastases [2]. Consequently, successful curative treatment depends on early diagnosis in an early stage. Because SCC in situ in the anal canal is frequently occurs as a slightly raised or flat lesion [3], it may be easily overlooked in a forward endoscopic view. During colonoscopy, the anal region should be carefully observed in a retroflexed view.

A search of the PubMed database retrieved only 5 case reports of SCC in the anal canal to date, all of which were treated by ESD (► **Table 1**) [4–6]. One case was positive for lymphovascular invasion and was treated by chemoradiation after ESD, but no recurrences were reported over an average follow-up of 14 mo (range: 3–23 mo) in all these cases. ESD is accepted as a minimally invasive treatment and offers benefits with respect to the quality of life of patients. It is a potential treatment option for SCC in situ in the anal canal. Only few cases of this type have been treated by ESD, and the long-term outcome is still unclear. Because there is no evidence that ESD is useful for the treatment of anal canal carcinoma in situ, careful follow-up is necessary.

Achievement of en bloc resection when performing ESD is important to prevent local recurrence, but it may be difficult to accurately determine the extent of the tumor margin. Chromoendoscopy with indigo carmine dye has been reported for the assessment of the lateral margin of early SCC in the anal canal [7], but this technique was not useful in our case (► **Fig. 1b**). The use of magnifying endoscopy with narrow-band imaging has been reported for detecting early SCC in the anal canal [4–6]. However, a magnifying endoscope does not have good operability during retroflexed observation in the lower rectum, and accurate evaluation of the margin of irregularly shaped flat lesions is difficult using narrow-band imaging without magnification. In our case, Lugol chromoendoscopy improved the visualization of high-grade intraepithelial neoplasia in the anal canal, and the irregularly shaped lesion was successfully resected en bloc by ESD (► **Fig. 2**). The whitish, slightly elevated lesion was stained by iodine because of parakeratosis, but the margin was clearly distinguished with WLI. Lugol chromoendoscopy is a

► **Table 1** Previous case reports treated with ESD.

	Age	Sex	Form	Size	Color	Depth	Lymphovascular invasion	HPV	Additional treatment	No recurrence
Ito	89	F	Slightly elevated	10 mm	Whitish	Tis	Ly0, v0	Not available	–	15 mo
Ito	66	F	Highly elevated	12 mm	Whitish	Tis	Ly1, v0	Not available	Chemoradiation	23 mo
Tsuji	60	F	Flat	20 mm	Reddish	Tis	Ly0, v0	Not available	–	3 mo
Ta-maruru	66	F	Slightly elevated	15 mm	Whitish	Tis	Ly0, v0	+	–	12 mo
Ta-maruru	71	F	Slightly elevated	25 mm	Whitish	Tis	Ly0, v0	+	–	19 mo
Our case	66	M	Slightly elevated	30 mm	Whitish	Tis	Ly0, v0	+	–	6 mo

simple technique that is easy to perform and can distinguish the lateral margin of dysplasia or neoplasia when used with WLI. In conclusion, patients with early SCC in the anal canal may benefit from ESD and Lugol chromoendoscopy, and careful follow-up is necessary.

Competing interests

None

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