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HPV-Related anal squamous papilloma serve as a red flag for potential anal squamous cell carcinoma: a case report

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Case Report

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Abstract

Background

Squamous cell carcinoma (SCC) of the anal canal is an uncommon malignancy related to HPV infection and is frequently challenging to identify at its early stage, owing to its inconspicuous morphology and poorly demarcated borders.

Case presentation

We present a case of a 57-year-old Chinese male who presented with two synchronous lesions located near the dentate line: a laterally spreading tumor (LST) and a separate flat, reddish lesion (type 0-IIb). Magnifying narrow-band imaging(NBI) revealed that the LST exhibited features consistent with squamous papilloma, while the flat lesion showed type B1 intra-papillary capillary loops（IPCL） suggestive of early SCC. Both lesions were completely resected *en bloc* by endoscopic submucosal dissection（ESD）. Subsequent histopathology confirmed papilloma in the LST and SCC limited to the lamina propria with clear margins.

Conclusions

This case suggests that the presence of squamous papilloma may indicate an increased likelihood of coexisting SCC in the anal canal. Careful and systematic evaluation using magnifying NBI, especially in individuals at elevated risk, may facilitate the detection of subtle early SCC lesions and allow for curative minimally invasive endoscopic treatment.

Background

SCC of the anal canal, particularly lesions developing on the oral side of the dentate line, is a rare malignancy and demonstrates clinicopathological similarities with those of SCCs arising in the esophagus and pharynx [1]. Owing to its inconspicuous morphology and poorly demarcated borders, early diagnosis of anal canal SCC is often difficult and depends on meticulous endoscopic assessment using enhanced imaging modalities [2]. Magnifying narrow-band imaging (M-NBI) enables detailed visualization of mucosal microvascular architecture, such as IPCL patterns, and has been shown to be useful for detecting superficial squamous neoplasia [3]. Notably, both anal canal SCC and squamous papilloma are associated with human papillomavirus (HPV) infection, implying a shared pathogenic mechanism [4]. While papilloma exhibits more distinct histopathological features, its presence may serve as an indicator for concurrent or underlying SCC. In this report, we describe a case of concurrent papilloma and SCC in the anal canal, both of which were successfully resected *en bloc* using ESD.

Case presentation

Patient Information

A 57-year-old male presented to our department with a one-week history of perianal itching. Digital rectal examination revealed a soft, raised mucosal lesion approximately 1.0 cm from the anal verge. The patient was subsequently admitted for further evaluation with colonoscopy. Physical examination following admission was unremarkable. Laboratory tests were positive for HPV types 16 and 18, and no other significant abnormalities were detected.

Diagnostic Assessment

Colonoscopy revealed a laterally spreading tumor (LST), approximately 2.0 cm in diameter, located about 1.0 cm superior to the dentate line (Fig. 1). Magnifying endoscopy showed the lesion to be pale in color. With indigo-carmine staining, the surface exhibited a sea anemone-like morphology, characterized by regular capillary arrangement within the mucosal villi. Within these structures, regular looped micro-vessels with an organized vascular pattern were observed. The previous endoscopic biopsy results of this lesion suggested a papilloma. While withdrawing the scope along the anal canal, an incidental finding was a patch of reddish, rough mucosa opposite the LST and adjacent to the dentate line. Upon careful withdrawal of the scope, this area was confirmed as a flat (0-IIb type), reddish, and granular lesion measuring approximately 1.5 x 2.0 cm (Fig. 2). The surface was soft, with no evident elevated or depressed components. A distinct demarcation line (DL) was also observed. Under narrow-band imaging (NBI), a brownish background was noted, and magnifying endoscopy revealed type B1 IPCL. Biopsy of this area confirmed high-grade intraepithelial neoplasia with carcinomatous change. Based on the findings, the lesions were clinically staged as cTis-cT1a. Given the indications, the patient was scheduled for ESD to resect both the LST and the 0-IIb type lesion.

Therapeutic Intervention

The lesions were resected completely following the standard ESD procedure, with negative margins confirmed. Histopathological examination revealed that the LST component corresponded to a squamous papilloma (Fig. 1). While the 0-IIb lesion was diagnosed as a superficial SCC measuring 1.0 × 1.5 cm, type 0-IIb, with invasion limited to the lamina propria mucosae (LPM), and negative horizontal (HM0) and vertical (VM0) margins, no lympho-vascular invasion (V0), and no lymphatic involvement (ly0) (Fig. 3, 4).

Follow-up and Outcomes

In follow-up procedure, the patient occasionally experienced anal discomfort and difficulty with defecation. At the one-month follow-up, mild anal stenosis was noted, which was subsequently managed with digital and balloon dilation. At the three-month follow-up, ulcer scar formation was observed at the resection site, and the patient was recovering well overall.

Discussion

The SCC of the anal canal is a rare epithelial malignancy and is a well-established HPV-related cancer associated with high-risk HPV types [5]. Given that HPV infection is found in 80–90% of anal SCCs, it is notable that in invasive anal cancers, HPV types 16, 18, and 31 are the most prevalent, with reported frequencies of 80.1%, 3.6%, and 1.9%, respectively [6]. Although the role of HPV in anal canal SCC has not been fully evaluated due to its rarity, one study reported an HPV positivity rate of 50% (5/10) in patient [7].

The squamous epithelium of the anorectal region extends from the transitional zone (between the dentate line and the pectinate/anal line) outward to the perianal skin [8]. The SCC originates specifically from the transitional zone of the anal canal, the length of which is less than 1 cm above the dentate line [9]. This area is physiologically narrowed by the anal sphincter complex, which often leads to suboptimal endoscopic visibility [10]. Consequently, it represents a visual blind spot and is prone to being overlooked during routine examination. Moreover, the SCC is often clinically identified at the carcinoma *in situ* stage, as its early morphological features are difficult to recognize endoscopically [11]. As with other malignant tumors, SCC of the anal canal has a poor prognosis after progression, making early detection crucial.

Given that HPV infection is the primary etiological factor for this disease, it is recommended that patients with identified risk factors—such as confirmed HPV infection, a history of receptive anal intercourse, HIV co-infection, or immunocompromised status—undergo routine and meticulous endoscopic examination of the anal canal [12]. Emerging evidence suggests that HPV infection is also closely associated with the development of papilloma in the digestive tract [13]. The initial finding in this reported case was a squamous papilloma, and it characterized by their distinct morphology, which is generally detectable at an early stage. Subsequent NBI examination of the dentate line region revealed an early-stage SCC. Given the SCC and squamous papilloma shared etiology and pathogenesis, the detection of squamous papilloma necessitates vigilant monitoring for concurrent superficial SCC to ensure comprehensive clinical evaluation. While the application of high-resolution endoscopy can improve the detection rate of anal SCC to some extent, its clinical utility remains limited [14]. Early endoscopic diagnosis of anal canal SCC is feasible and can be enhanced by careful forward-view inspection during insertion and systematic retroflexion in the rectum. For high-risk patients, we propose that routine NBI examination combined with magnifying endoscopy of the anal verge should be performed prior to concluding the colonoscopy procedure [15]. In superficial anal canal carcinoma, the proliferating microvascular within the tumor lesion are morphologically distinct from normal microvascular, which allows the tumor region to be identified as a brownish area under imaging [3]. In the present case, magnifying NBI endoscopy showed the dilatated, tortuous and caliber changed vascular pattern of IPCL, which suggested that the lesion was a SCC of anal canal.

In conclusion, improving the diagnosis of anal canal SCC requires a strategy that combines endoscopic vigilance with clinical risk stratification. The finding of a squamous papilloma should alert the endoscopist to the possibility of an underlying SCC. Magnifying NBI is essential in this setting, as it can

delineate early neoplastic microvascular changes—notably dilated and tortuous IPCLs. Interpreting these imaging features within the context of a patient's HPV-associated risk profile, including specific factors such as HPV infection, sexual history, HIV status, and immunodeficiency, further sharpens diagnostic accuracy. Together, this integrated approach promotes earlier detection, which is critical given the poor prognosis of advanced disease.

Abbreviations

DL Demarcation line

ESD Endoscopic submucosal dissection

HPV Human papillomavirus

IPCLs Intra-papillary capillary loops

LPM Lamina propria mucosae

LST Laterally spreading tumor

M-NBI Magnifying Narrow-band imaging

NBI Narrow-band imaging

SCC Squamous cell carcinoma

Declarations

Ethics approval and consent to participate

As this is a single patient case report, formal ethics committee approval was not required. Written informed consent to participate was obtained from the patient.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

All data supporting the findings of this report are contained within the article. No additional datasets were generated or analyzed.

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

Conceptualization and Writing-original draft preparation, Xiaoxiang Wang; Methodology and Writing—review and editing, Xudong Wen; Investigation, Hongmei Wang; Supervision, Tao Pan

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Not applicable.

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Figures

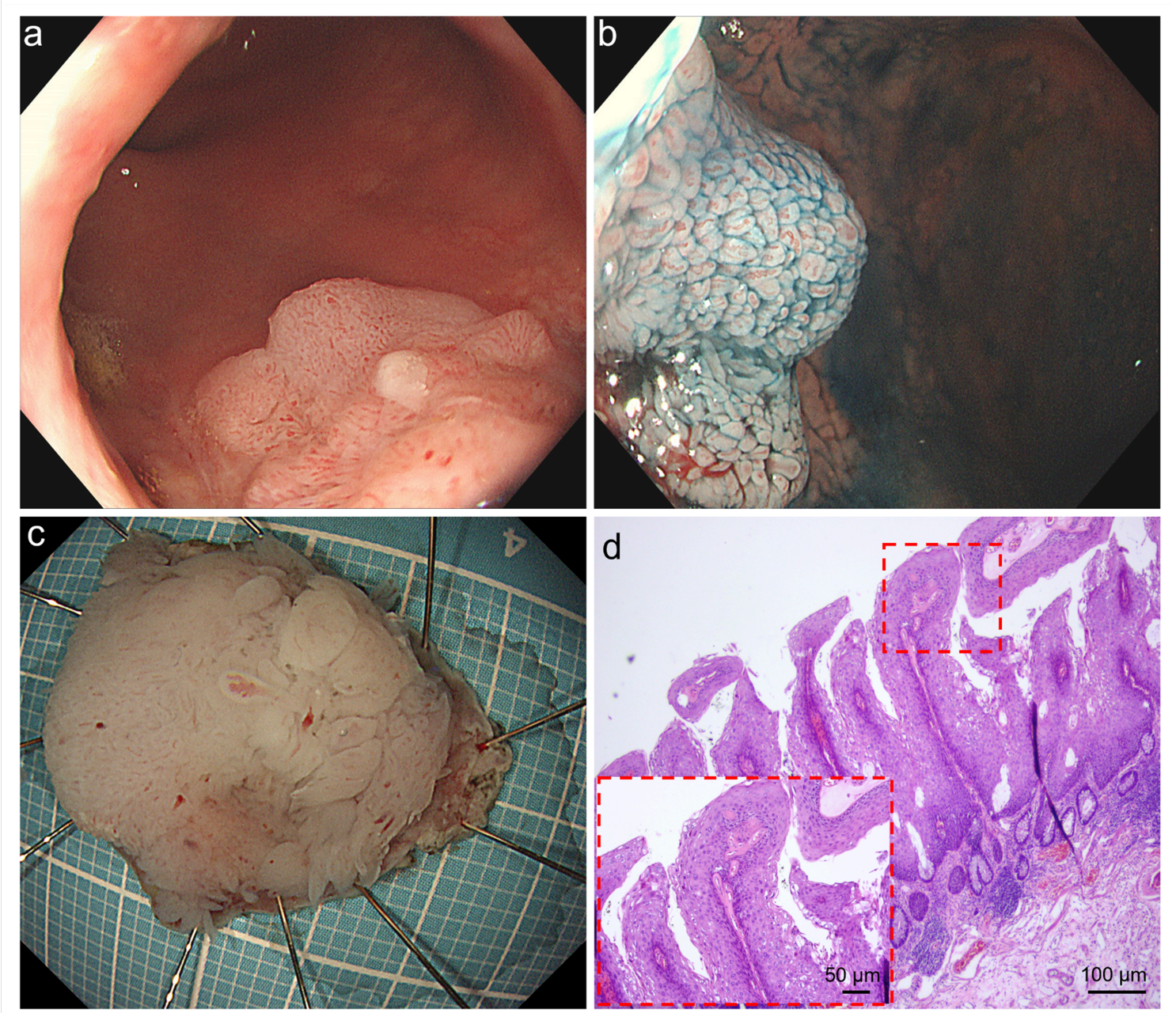


Figure 1

Diagnosis and treatment of squamous epithelial papilloma. **a** A papilloma lesion is identified 1 cm superior to the dentate line. **b** Indigo carmine staining displays appeared sea anemone-like, and the regular arrangement of capillaries could be observed within the mucosal villi. **c** ESD is performed for complete resection of papilloma lesion. **d** Pathological examination reveals exophytic papillary hyperplasia of the squamous epithelium, featuring hyperchromatic nuclei in the epithelial cells, hyperkeratosis, and terminal spiking.

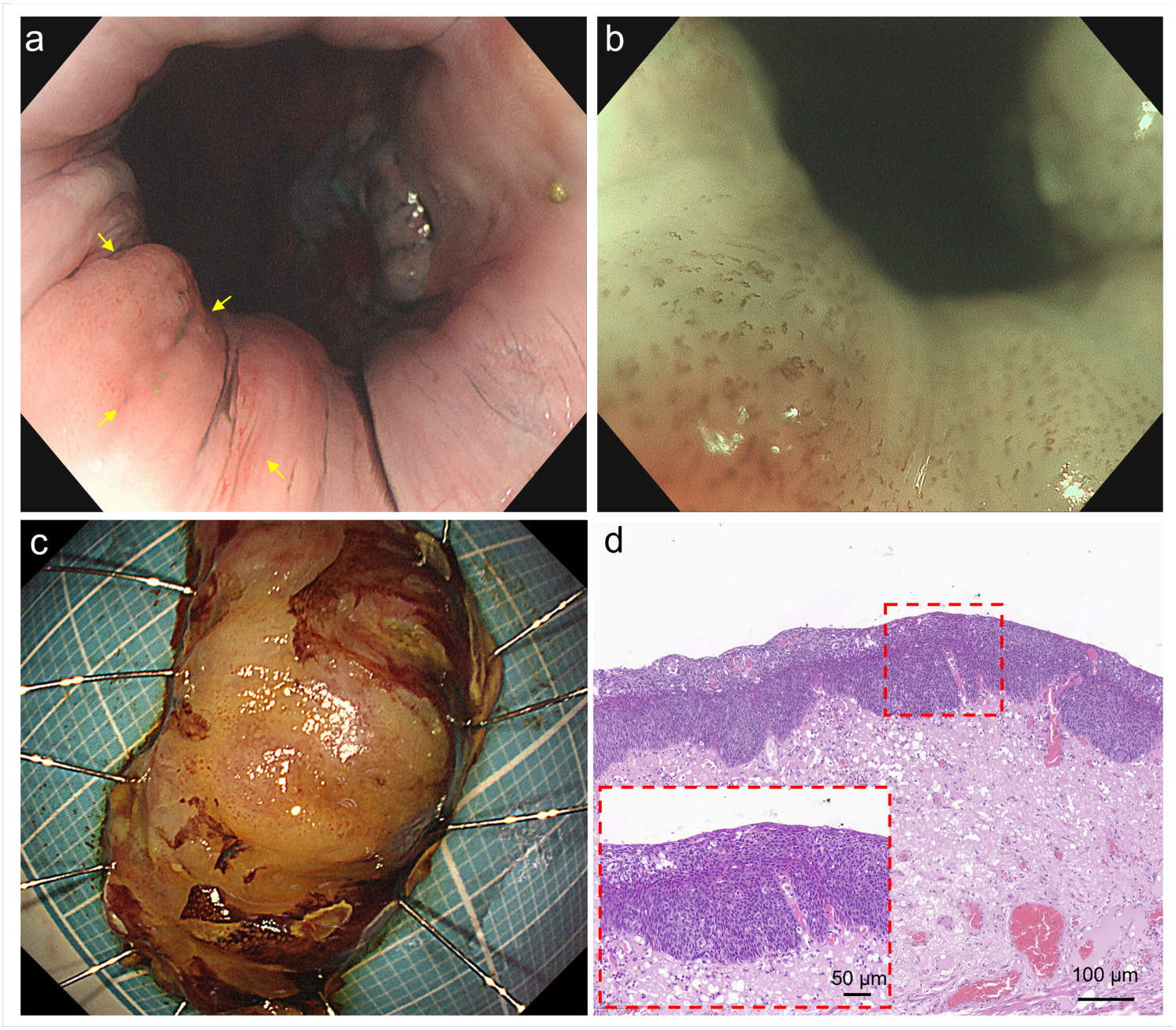


Figure 2

Diagnosis and treatment of superficial squamous carcinoma. **a**Along the anal canal, an inconspicuous lesion (flat, erythematous) is found at the dentate line (yellow arrows). **b** Under NBI magnification, a type 0-IIb brownish area with a clear demarcation line is identified and type B1 IPCLs are observed. **c** The flat lesion is completely resected using ESD. **d** Post-resection pathology confirms that the flat lesion is diagnosed as a superficial squamous cell carcinoma (1.0 × 2.5 cm, type 0-IIb, LPM, V0, ly0).

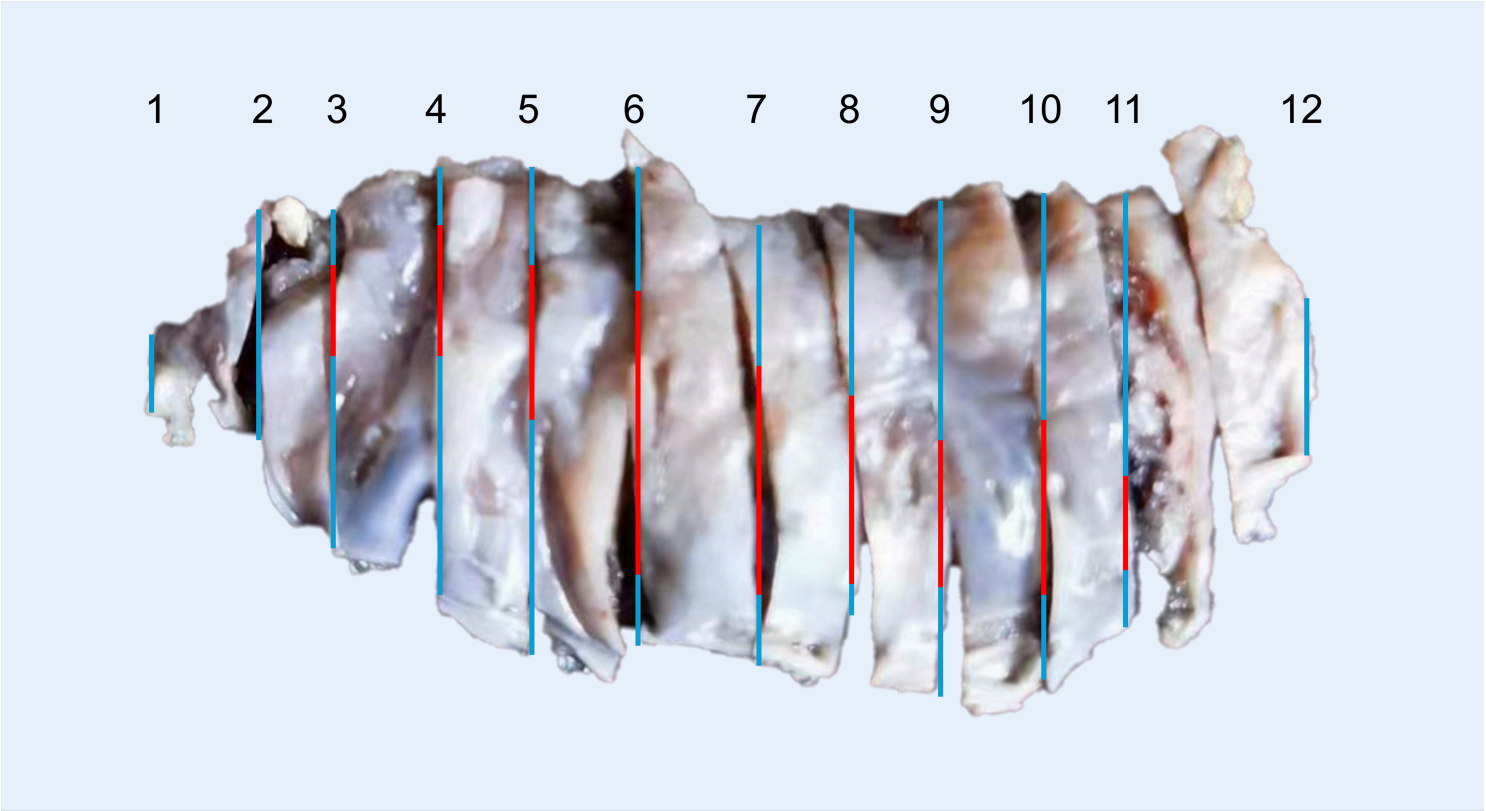


Figure 3

Pathological gross specimen reconstruction image following endoscopic submucosal dissection of anal canal superficial squamous cell carcinoma. The lesion is sectioned into 12 tissue strips, with red highlighting areas of the lesion and blue demarcating normal tissue.

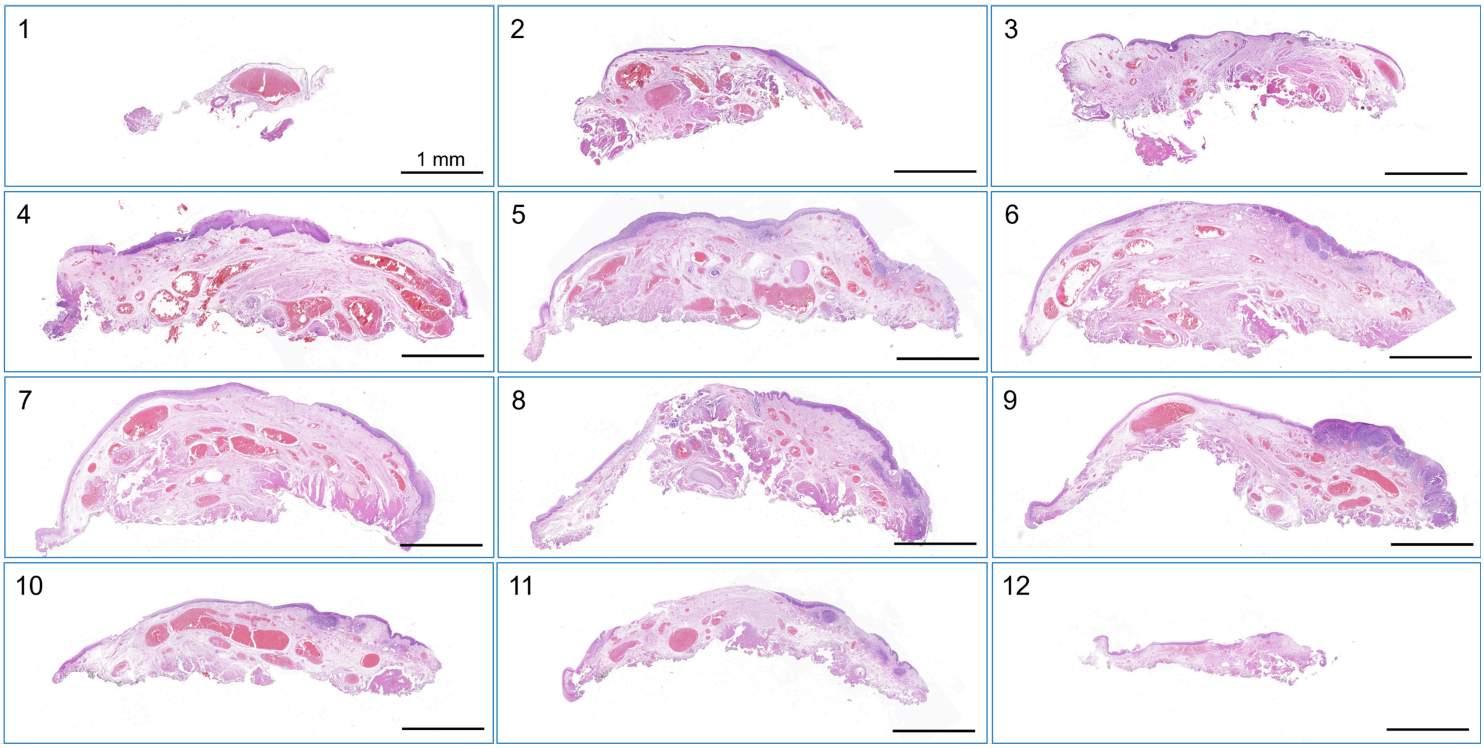


Figure 4

Representative pathological of anal canal squamous cell carcinoma from an endoscopic submucosal dissection specimen sectioned into 12 tissue strips.