

# World Journal of *Clinical Cases*

*World J Clin Cases* 2019 July 6; 7(13): 1535-1731





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*World Journal of Clinical Cases* (*World J Clin Cases*, *WJCC*, online ISSN 2307-8960, DOI: 10.12998) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

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**INDEXING/ABSTRACTING**

The *WJCC* is now indexed in PubMed, PubMed Central, Science Citation Index Expanded (also known as SciSearch®), and Journal Citation Reports/Science Edition. The 2019 Edition of Journal Citation Reports cites the 2018 impact factor for *WJCC* as 1.153 (5-year impact factor: N/A), ranking *WJCC* as 99 among 160 journals in Medicine, General and Internal (quartile in category Q3).

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Responsible Electronic Editor: *Yan-Xia Xing*

Proofing Production Department Director: *Yun-Xiaojuan Wu*

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Semimonthly

**EDITORS-IN-CHIEF**

Dennis A Bloomfield, Sandro Vento

**EDITORIAL BOARD MEMBERS**

<https://www.wjnet.com/2307-8960/editorialboard.htm>

**EDITORIAL OFFICE**

Jin-Lei Wang, Director

**PUBLICATION DATE**

July 6, 2019

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**PUBLICATION MISCONDUCT**

<https://www.wjnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Endoscopic submucosal dissection as excisional biopsy for anorectal malignant melanoma: A case report

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**Author contributions:** Manabe S was responsible for the patient, performed endoscopic submucosal dissection, and drafted the manuscript; Boku Y performed endoscopic examination; Takeda M, Usui F, Hirata I and Takahashi S proofread and revised the manuscript; all authors approved the final version of the manuscript.

**Informed consent statement:** The patient was offered written explanations before the start of the treatment, and she provided consent.

**Conflict-of-interest statement:** The authors declare that there is no conflict of interest.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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### Abstract

#### BACKGROUND

Anorectal malignant melanoma (AMM) is a rare disorder with an extremely poor prognosis. Although there is currently no consensus on the treatment methods for AMM, surgical procedures have been the most common treatment methods used until now. We recently encountered a case of AMM that we diagnosed using endoscopic submucosal dissection (ESD). To our knowledge, this is the first case of ESD for AMM, suggesting that ESD can potentially be a diagnostic and treatment method for AMM.

#### CASE SUMMARY

A 77-year-old woman visited our hospital with a chief complaint of anal bleeding and a palpable rectal mass. Colonoscopy revealed a 20-mm protruded lesion in the lower rectum. After obtaining biopsy specimens from the lesion, although a malignant rectal tumor was suspected, a definitive diagnosis was not made. Endoscopic ultrasonography revealed tumor invasion into the submucosal layer but not the muscular layer. Therefore, we performed an excisional biopsy using ESD. Immunohistochemical examination of the ESD-resected specimen revealed tumor cells positive for Human Melanin Black-45, Melan-A, and S-100. Moreover, the tumor cells lacked melanin pigment; thus, a diagnosis of amelanotic AMM was made. Although the AMM had massively invaded the submucosal layer and both lymphatic and venous invasion were present, we closely monitored the patient without any additional therapy on the basis of her request. Six months after ESD, local recurrence was detected, and the patient consented to wide local excision.

#### CONCLUSION

It is suggested that ESD is a potential diagnostic and treatment method for AMM.

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**Manuscript source:** Unsolicited manuscript

**Received:** March 2, 2019

**Peer-review started:** March 2, 2019

**First decision:** March 29, 2019

**Revised:** April 15, 2019

**Accepted:** May 2, 2019

**Article in press:** May 2, 2019

**Published online:** July 6, 2019

**P-Reviewer:** de Moura DTH, Lim SC, Shin SJ

**S-Editor:** Gong ZM

**L-Editor:** A

**E-Editor:** Wang J



**Key words:** Endoscopic submucosal dissection; Anorectal malignant melanoma; Endoscopic mucosal resection; Case report

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**Core tip:** For anorectal malignant melanoma (AMM), surgical procedures such as abdominoperineal resection and wide local excision have been the most common treatment methods used until now. We recently encountered a case in which endoscopic submucosal dissection (ESD) was used for an excisional biopsy of AMM. ESD may be effective for an early and accurate AMM diagnosis because the ESD-resected specimen could provide adequate pathological findings. In addition, as the ESD technique can yield a high en bloc resection rate, ESD may effectively treat early-stage AMM. Thus, it is suggested that ESD is a potential diagnostic and treatment method for AMM.

**Citation:** Manabe S, Boku Y, Takeda M, Usui F, Hirata I, Takahashi S. Endoscopic submucosal dissection as excisional biopsy for anorectal malignant melanoma: A case report. *World J Clin Cases* 2019; 7(13): 1652-1659

**URL:** <https://www.wjgnet.com/2307-8960/full/v7/i13/1652.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v7.i13.1652>

## INTRODUCTION

Anorectal malignant melanoma (AMM) is a rare disease, accounting for less than 1% of all melanomas and approximately 1% of carcinomas arising from the anorectal region. The prognosis of AMM is extremely poor, with a median survival of 24 mo and a 5-year survival rate of 10%<sup>[1]</sup>. Clinical manifestations are non-specific<sup>[2]</sup>, and the histological features of AMM overlap with those of other tumors, such as sarcoma, lymphoma, and undifferentiated carcinoma<sup>[3]</sup>. These non-specific clinical features contribute to delayed diagnosis, and almost 60% of patients are diagnosed with metastatic lesions at initial diagnosis<sup>[4]</sup>. Although surgical procedures such as abdominoperineal resection (APR) and wide local excision (WLE) have been the mainstay treatments for AMM<sup>[5]</sup>, increasing evidence suggests that the surgical method affects the local recurrence rate but not survival outcomes<sup>[6,7]</sup>. On the other hand, less invasive therapies such as endoscopic mucosal resection (EMR) may be effective for early-stage AMM<sup>[8,9]</sup>.

We recently encountered a case in which endoscopic submucosal dissection (ESD) was used for an excisional biopsy of AMM. To our knowledge, this is the first case of ESD for AMM. Given that our case suggests the efficacy of ESD as an excisional biopsy for AMM, we present this case with a brief review of the literature.

## CASE PRESENTATION

### Chief complaints

A 77-year-old woman visited our hospital with a chief complaint of anal bleeding and a palpable rectal mass.

### History of present illness

Anal bleeding and a palpable rectal mass were observed one month before presentation.

### History of past illness

The patient had no notable previous medical history.

### Physical examination

Digital rectal examination revealed a nodular mass just above the dentate line.

### Laboratory examinations

Blood analysis revealed that tumor markers, including carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9, were within the normal range (CEA level of 1.7 ng/mL and CA19-9 level of 13.9 U/mL). Complete blood count and results



from blood biochemical analysis were normal.

### **Imaging examinations**

Total colonoscopy revealed no abnormality in the colon. However, it revealed a 20-mm protruded lesion in the lower rectum just above the dentate line, which was thought to be the cause of the patient's chief complaint (Figure 1). Narrow-band imaging with magnifying endoscopy (NBI-ME) revealed non-structural areas and some thick, unevenly sized vessels with branching and curtailed irregularity (Figure 2). Endoscopic ultrasonography (EUS) revealed the tumor invading the submucosal layer but not the muscular layer (Figure 3). Contrast-enhanced computed tomography (CECT) and fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) showed no lymph nodes or distant metastases.

### **Further diagnostic work-up**

Biopsy specimens of the lesion showed diffuse infiltration of round atypical cells with irregular nuclei. On the basis of the endoscopic findings and histopathological examination of the biopsy specimens, a malignant rectal tumor, including adenocarcinoma, neuroendocrine tumor, and malignant lymphoma, was suspected. However, we could not make a definite diagnosis regardless of several sufficiently sized biopsy specimens. In addition, since this lesion was expected to have invaded the submucosal layer on the basis of EUS findings, endoscopic therapy alone was considered insufficient. However, considering that this lesion was located in the lower rectum, we believed that ESD would be a better first choice as an excisional biopsy than other surgical procedures that would be highly invasive. Therefore, we performed an excisional biopsy *via* ESD instead of re-performing biopsy using forceps. Histopathological examination of the ESD-resected specimen revealed diffuse infiltration of round tumor cells with irregular nuclei (Figure 4A). Additionally, immunohistochemical examination revealed tumor cells positive for Human Melanin Black-45, Melan-A, and S-100 (Figure 4B-D). In addition, the tumor cells lacked melanin pigment; thus, a diagnosis of amelanotic AMM was made. Although all margins of the ESD-resected specimen were free from melanoma cells, the AMM had invaded the submucosal layer up to 7000  $\mu$ m, and both lymphatic and venous invasion were noted.

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## **FINAL DIAGNOSIS**

On the basis of the histopathological findings of the ESD-resected specimen, a diagnosis of amelanotic AMM was made.

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## **TREATMENT**

ESD as an excisional biopsy was performed using a colonoscope (CF-Q260AI; Olympus Corporation, Tokyo, Japan), Flush Knife BT-S (DK2620J, FUJIFILM Medical, Tokyo, Japan), and high-frequency generator unit (VIO300D, Erbe Elektromedizin GmbH, Tuebingen, Germany).

First, as the tumor was located very close to the dentate line, we injected lidocaine solution into the submucosal layer to prevent the patient's pain during the procedure. Subsequently, we started the mucosal incision from the anal side of the lesion. After creating a mucosal flap, we performed mucosal incision of the entire circumference around the lesion with an adequate margin and continued with submucosal dissection. No non-lifting sign was observed during ESD. The operation time was 62 min, and the lesion was resected en bloc without any complications. The ESD-resected specimen and the tumor measured 40 mm  $\times$  30 mm and 20 mm  $\times$  15 mm, respectively (Figure 5). The patient was discharged on postoperative day 4.

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## **OUTCOME AND FOLLOW-UP**

After obtaining the histopathological results of the ESD-resected specimen, we recommended additional surgical treatment, such as APR or WLE, with adjuvant chemotherapy. However, the patient and her family requested observation without any additional therapy because of the advanced age of the patient, high invasiveness and lack of proven efficacy of the suggested therapies, and a small chance of no recurrence. Therefore, we closely monitored the patient by endoscopic examination, CECT, and FDG PET/CT, as requested. During the 6-mo follow-up period, the patient



**Figure 1 Colonoscopic findings.** A 20-mm protruded lesion in the lower rectum just above the dentate line is detected.

was asymptomatic, and there was no evidence of recurrence (Figure 6). However, 6 mo after ESD, local recurrence was detected on endoscopic examination (Figure 7), following which the patient and her family finally consented to WLE.

## DISCUSSION

AMM is a rare disorder arising from melanocytes in the mucosa around the anorectal region, and its prognosis is extremely poor<sup>[1]</sup>. The 5-year survival rate varies according to the presence of metastasis. The 5-year survival rate when AMM is confined to a local area has been reported to be 32%, whereas that in the presence of regional or distant disease decreases to 17% or 0%, respectively<sup>[10]</sup>. However, as high as 60% of patients are diagnosed with metastatic lesions at initial diagnosis<sup>[4]</sup>.

Given that AMM is rare and its clinical features lack specificity, the rate of misdiagnosis is high (57.14%–58.23%)<sup>[7,11]</sup>; this, in turn, may lead to its delayed diagnosis and poor prognosis. Further, amelanotic AMM, which accounts for approximately 20% of AMM cases<sup>[6]</sup>, is more likely to be misdiagnosed. The causes for misdiagnosis include the lack of sufficient knowledge about this disease among endoscopists, the lack of specific clinical features, and the difficulty in its pathological diagnosis. Especially, an accurate diagnosis of amelanotic AMM could not be established without immunohistochemical examination<sup>[7]</sup>. In our case, a diagnosis of amelanotic AMM was not established based on the NBI-ME, EUS, and histopathological examination of the biopsy specimens, which were performed before ESD. It was only after the excisional biopsy via ESD that we were able to diagnose amelanotic AMM. Thus, ESD was essential in establishing the diagnosis of amelanotic AMM in this particular case.

Although there is currently no consensus on the treatment methods for AMM because of its infrequency and poor biological behavior, surgical procedures such as APR and WLE have been the most common treatment methods used until now<sup>[3]</sup>. Additionally, there has been a long-standing debate regarding whether APR or WLE is better in terms of long-term survival and quality of life. Although designing a prospective, large-scale study is unrealistic because of the low incidence of AMM, some studies have suggested that there are no significant differences in survival outcomes between patients treated with APR and those treated with WLE and that APR is superior to WLE only in terms of the local recurrence rate despite the high invasiveness of APR<sup>[6,7]</sup>. Therefore, considering the extremely poor prognosis of AMM and that local recurrence could be controlled by salvage surgery, WLE may be a better first-choice surgical procedure for AMM than APR.

On the other hand, recently, only a few cases of AMM have been treated with EMR<sup>[8,9]</sup>; the advantage of this procedure is that it is much less invasive than conventional surgical procedures. Moreover, these cases suggest that early-stage AMM could be managed by endoscopic therapy alone. Compared with EMR, the ESD technique can yield a high en bloc resection rate for a lesion, irrespective of its size or shape<sup>[12]</sup>. Therefore, compared to EMR, ESD could more effectively treat early-stage AMM. Indeed, ESD was applied to a few cases of esophageal malignant melanomas, and long-term survival was achieved in these cases<sup>[13,14]</sup>. However, to our knowledge, this is the first case of ESD for AMM.

Unfortunately, in this particular case, as the AMM had massively invaded the submucosal layer, and as both lymphatic and venous invasion were present, the possibility of recurrence or distant metastasis was speculated to be extremely high,





**Figure 2** Narrow-band imaging with magnifying endoscopy findings. Non-structural areas and some thick, unevenly sized vessels with branching and curtailed irregularity are observed.

and ESD alone was considered insufficient therapy. Indeed, local recurrence occurred, and the patient subsequently underwent WLE. However, we were able to establish the diagnosis of AMM correctly from the ESD-resected specimen and were able to present the option of additional therapy to the patient subsequently.

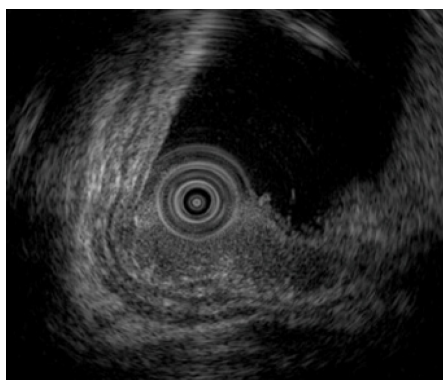
Thus, although early diagnosis of AMM may contribute to definitive resection and better survival outcomes, prompt and accurate diagnosis of AMM is difficult, leading to a high incidence of locally advanced or metastatic lesions at the time of diagnosis<sup>[15]</sup>. In those cases, ESD may be effective for an early and accurate diagnosis of AMM, as the ESD-resected specimen could provide adequate pathological findings, compared to biopsy specimens, for pathologists to arrive at a diagnosis of AMM. In addition, compared to EMR, the ESD technique can yield a high en bloc resection rate. Further, it is relatively easier to perform ESD for lower rectal lesions than for lesions located in other parts of colon, and perforation does not occur as long as the lesion is located under the level of peritoneal reflection. Therefore, ESD could be a relatively safe and better endoscopic treatment method than EMR for early-stage AMM. Thus, it is suggested that ESD is a potential diagnostic and treatment method for AMM.

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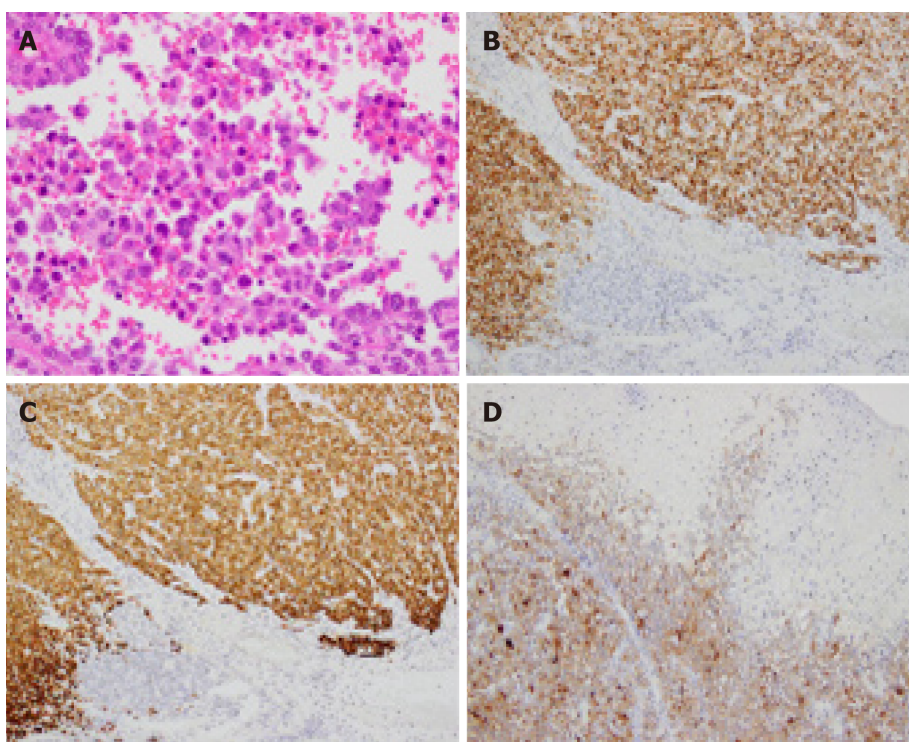
## CONCLUSION

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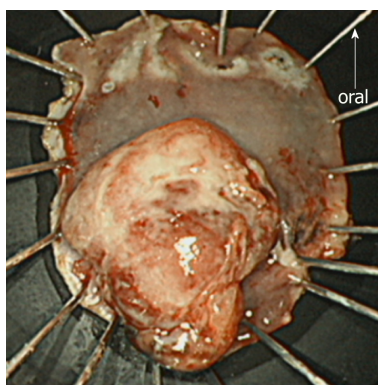
This case report highlights the efficacy of ESD as an excisional biopsy for AMM. This case suggests that ESD is effective in establishing a diagnosis of AMM because the ESD-resected specimen could provide adequate pathological findings to make a diagnosis of AMM. In addition, as the ESD technique can yield a high en bloc resection rate, ESD could be one of the endoscopic treatment methods for early-stage AMM. Further cases are needed to confirm the efficacy and limitations of ESD for AMM.



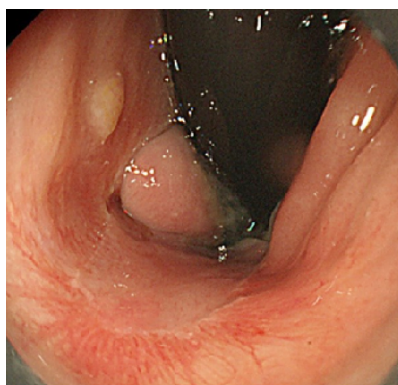
**Figure 3 Endoscopic ultrasonography findings.** Endoscopic ultrasonography image shows the lesion as a hypoechoic mass. The tumor invades the submucosal layer but not the muscular layer.



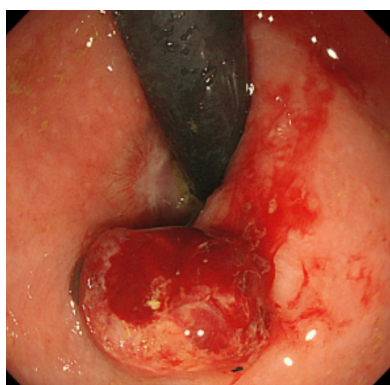
**Figure 4 Histopathological and immunohistochemical findings of the endoscopic submucosal dissection-resected specimen.** A: Hematoxylin and eosin staining shows diffuse infiltration of round tumor cells with irregular nuclei. Melanin pigment is absent (magnification  $\times 400$ ). The tumor cells are positive for B: Human Melanin Black-45 ( $\times 200$ ), C: Melan-A ( $\times 200$ ), and D: S-100 ( $\times 100$ ).



**Figure 5 Endoscopic submucosal dissection-resected specimen.** The endoscopic submucosal dissection-resected specimen is  $40 \times 30$  mm in size. The tumor is protruded and measures  $20 \times 15$  mm. Macroscopically, an adequate margin from the tumor, especially on the oral side, is ensured.



**Figure 6** Follow-up endoscopic findings 3 mo after the endoscopic submucosal dissection. The post-endoscopic submucosal dissection ulcer is healed, and no local recurrence is detected.



**Figure 7** Follow-up endoscopic findings 6 mo after the endoscopic submucosal dissection. A 10-mm protruded lesion is identified about 10 mm from the oral side of the post-endoscopic submucosal dissection scar. Biopsy specimens from this lesion confirm a malignant melanoma.

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