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ABOUT COVER
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AIMS AND SCOPE
The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING
The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJCC as 1.1; IF without journal self cites: 1.1; 5-year IF: 1.3; Journal Citation Indicator: 0.26; Ranking: 133 among 167 journals in medicine, general and internal; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE
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Endoscopic ultrasound features of rectal melanoma: A case report and review of literature

Zhang-E Xiong, Xin-Xiang Wei, Li Wang, Chen Xia, Zi-Yin Li, Chan Long, Bo Peng, Ting Wang

Abstract

BACKGROUND
Rectal mucosal melanoma is a rare and highly aggressive disease. Common symptoms include anal pain, an anal mass, or bleeding. As such, the disease is usually detected on rectal examination of patients with other suspected anorectal diseases. However, due to its rarity and nonspecific symptoms, melanoma of the rectal mucosa is easily misdiagnosed.

CASE SUMMARY
This report describes the case of a 58-year-old female patient who presented with a history of blood in her stool for the prior one or two months, without any identifiable cause. During colonoscopy, a bulge of approximately 2.2 cm × 2.0 cm was identified. Subsequently, the patient underwent endoscopic ultrasound (EUS) to characterize the depth of invasion of the lesions. EUS suggested a hypoechoic mucosal mass with involvement of the submucosal layer and heterogeneity of the internal echoes. Following surgical intervention, the excised tissue samples were examined and confirmed to be rectal malignant melanoma. The patient recovered well with no evidence of recurrence during follow-up.

CONCLUSION
This case shows that colonoscopy with EUS and pathological examination can accurately diagnose rare cases of rectal mucosal melanoma.

Key Words: Endoscopic ultrasound; Rectal mucosal melanoma; Colonoscopy; Treatment;
Core Tip: Rectal mucosal melanoma is an exceptionally rare cancer that is more aggressive than other melanomas of the same stage. Its vague symptoms, such as anal pain or rectal bleeding, especially in the early stages, lead to common misdiagnoses of hemorrhoids and colorectal cancer due to its lack of melanin manifestations and hyperpigmentation. In this case report, we described a diagnostic process through different endoscopic and imaging examinations.

INTRODUCTION
Rectal mucosal melanoma is a rare form of melanoma, accounting for only 1% to 2% of melanomas. Endoscopic ultrasound (EUS) provides a better assessment of the depth of infiltration than computed tomography (CT) or magnetic resonance imaging (MRI), which makes it more useful for evaluating clinical staging and selecting surgical methods. In this article, we present the case of a patient with a rarely observed rectal mucosal melanoma and a literature review of the topic.

CASE PRESENTATION
Chief complaints
A 58-year-old woman presented to our outpatient anorectal surgery clinic with a history of blood in her stools for the prior one or two months with no apparent cause.

History of present illness
Once a day for the previous month, the patient had produced soft stools that had a small amount of blood adhering to the surface of the stool as well as a small amount of mucus. However, the patient denied any other symptoms connected to the digestive system, including stomach pain, pus and blood in the stool and loss of appetite.

History of past illness
The patient had a history of bronchitis, esophagitis, and gastric ulcers. She had undergone surgery for a compression fracture of the lumbar spine (L2) in June 2018 (details unknown).

Personal and family history
The patient had no family history of rectal malignant melanoma or of psychological or genetic disorders.

Physical examination
After admission, relevant auxiliary examinations were performed, and the patient had no further abnormal signs. Her general condition was good, and her vital signs were within physiologic limits.

Laboratory examinations
Laboratory examinations revealed that the patient’s bloodwork was within normal limits. Stool routine tests were positive for (+) occult blood.

Imaging examinations
A bulging tumor of approximately 2.2 cm × 2.0 cm with a purplish-red apex and clear boundaries was identified approximately 8 cm from the anus by colonoscopy (Figure 1). EUS suggested a hypoechoic mucosal mass with involvement of the submucosal layer and heterogeneity of the internal echoes (Figure 2A-E). Color Doppler showed localized blood, and the intrinsic muscle layer was still intact (Figure 2F). Abdominopelvic CT indicated nodular enhancement foci in the rectum, and fortunately, no definitively enlarged lymph nodes or metastatic foci were identified throughout the abdomen (Figure 3).
A bulging tumor of approximately 2.2 cm × 2.0 cm with a purplish-red apex and clear boundaries was identified approximately 8 cm from the anus by colonoscopy.

Figure 1

Endoscopic ultrasound image and color Doppler image. A-E: Endoscopic ultrasound image showing a hypoechoic mucosal mass with involvement of the submucosal layer and heterogeneity of the internal echoes; F: Color Doppler showed localized blood with the intrinsic musculature still intact.

Figure 2

Final Diagnosis

Local biopsy for pathology and immunohistochemistry showed positivity for HMB45 and S-100 (Figure 4), and the results verified that the tumor was a rectal malignant melanoma.

Treatment

The patient was subsequently transferred to another hospital for wide local excision (LE) and received temozolomide combined with cisplatin adjuvant chemotherapy.
OUTCOME AND FOLLOW-UP
No local lymph node metastasis was observed either surgically or pathologically. The patient underwent surgical treatment and was followed up for 2 years, with no recurrence or metastasis exhibited.

DISCUSSION
The incidence rate of malignant melanoma is 21.9-55.9 per 100000 people in Western countries[1] and 0.2-0.65 per 100000 people in Asia[2]. It is commonly held that the development of melanoma is associated with intermittent high-intensity ultraviolet (UV) light exposure, genetics and other factors[3]. UV radiation may induce melanoma through direct mutagenic effects on DNA, stimulation of skin cells to produce growth factors and other effects[4]. However, in Asian populations, the primary foci of malignant melanoma are usually located in the heel, metacarpal, and subungual areas that are seldom exposed to UV radiation[1,5-7], which indicates that the development of malignant melanoma is not related to UV radiation. Indeed, the cause may be related to trauma and regions of physical stress[8,9]. In 2018, the World Health Organization classified melanomas into sun-related etiologies and non-sun-related melanomas, determined by their mutational features, anatomical sites and epidemiology. Sun-related melanomas include superficial diffuse melanoma, malignant freckle-like maculopathy and connective hyperplastic melanoma. The "nonsunlight" category includes melanomas of the extremities, some melanomas in congenital nevi, melanomas in blue nevi, Spitz melanomas, mucosal melanomas (MM), and uveal melanomas[10]. This discussion focuses on MM. Primary mucosal melanoma was identified for the first time in 1859 by Weber[11]. Mucosal melanoma is an extremely rare illness. The incidence of mucosal melanoma varies relatively significantly among different ethnic groups. Among the Caucasian population, MM account for approximately 1%-2% of all melanomas. However, the incidence of this disease is as high as 22.6% in China, which may be related to the lower incidence of cutaneous melanoma in China[12]. The main primary sites of MM in China are the nasal cavity, oral cavity, anorectum and genitourinary tract[13,14]. Due to their insidious location, these lesions usually present with bleeding, pain or discomfort as they form large tumors that invade and destroy surrounding tissues[10]. Malignant MM are more aggressive and have a worse prognosis than melanomas of other organs. Moreover,
Melanocytes are specialized cells whose primary role is to produce melanin, which acts as a barrier to protect DNA from UV radiation. Skin melanocytes are derived from dorsally migrating neural crest cells and ventrally migrating neural precursor cells. Most melanocytes of ectoderm origin in vertebrates are located in the epidermis and dermis of the skin; however, they are also present in many other locations, including the eye, mucous membranes, and soft brain membranes. Melanocytes of endodermal origin account for a small proportion of melanocytes, such as those in the nasopharynx, larynx, trachea bronchus and esophagus, which may explain the difference in the incidence of melanomas of the two different origins. Furthermore, these cells are often found at the mucocutaneous junction and were once thought to be responsible for the extended formation of melanin in the skin. The presence of melanocytes has been demonstrated in mucous membranes; however, the role and function of mucosal melanocytes appear to be unclear.

MM mainly include mucosal melanoma of the head and neck, mucosal melanoma of the female genitalia and mucosal melanoma of the gastrointestinal tract (MMG).

MMGs can arise in any area of the gastrointestinal tract, but most usually originate from the anal canal (31.4%), rectum (22.2%), stomach (2.7%), oropharynx (2.3%), small bowel (2.3%), gallbladder (1.4%) or colon (0.9%). Esophageal melanoma can cause severe dysphagia due to ulceration but can also lead to retrosternal pain, weight loss, and, in rare cases, vomiting blood or black stools. Symptoms of gastric mucosal melanoma are nonspecific and include abdominal pain, weight loss, upper gastrointestinal bleeding and anemia. Melanoma of the small intestinal mucosa is most often secondary to metastases from melanoma of the gastrointestinal tract and usually presents with nausea, vomiting, anorexia, abdominal pain, weight loss, gastrointestinal hemorrhage with secondary anemia and intussusception. Symptoms of anorectal melanoma include blood in the stool, anal pain or discomfort, and anal mass or prolapse of a rectal mass. The challenge in diagnosing MMG is that its early symptoms are usually insidious and nonspecific. Especially in the early stages, the lack of melanin discoloration and melanin deposition leads to misdiagnosis.

The definitive diagnosis of mucosal melanoma relies on histopathological and immunohistochemical findings. Biopsy of the lesion is followed by histopathological and immunohistochemical examination to establish the diagnosis. Melanoma has a wide range of histological features resembling epithelial, hematological, mesenchymal and neural tumors. The primary lesion is characterized by nests and single growths of atypical melanocytes in the surrounding mucosa. Other histopathological features of mucosal melanoma include frequent vascular infiltration and multicentricity. Immunohistochemistry is the main tool used to differentiate melanoma from other tumors. Similar to methodologies used for cutaneous melanoma, MM differentially express S-100 proteins and melanocyte markers, including MART1/Melan-A, HMB-45, tyrosinase and MITF. Approximately half of MM patients carry BRAF mutations that provide loci for targeted therapies.

Clinical staging of mucosal melanoma is crucial for determining the extent of the disease and guiding treatment decisions. There are two staging methods for anorectal melanoma: (1) These methods were developed by the American Joint Committee on Cancer and are commonly used in clinical practice. This is a staging method based on the depth of the primary tumor; the lesion is confined to the mucosal layer, located in the submucosa, and infiltrates into the muscular layer. The deeper the lesion infiltration is, the greater the risk of lymph node metastasis; and (2) The other staging system is based on the spread of the disease only: localized disease only is described as stage I, regional lymph node disease as stage II and metastatic disease as stage III.

We collected eight chart reports of primary rectal mucosal melanoma during the last 6 years; most of which involved female patients; most of these patients were seen for rectal bleeding (62.5%), anal masses (37.5%), and discomfort or pain during defecation (25%). There was one case of distant metastasis, and the remaining cases were mostly confined to the bowel wall.

The mainstay of treatment for MM remains surgery. In the collected case reports, most patients without distant and lymph node metastases and peripheral spread were treated by LE when local and lymph node metastases were present, traditional abdominal perineal resection (APR) was still used. Traditionally, the surgical treatment of rectal-anal melanoma has been APR because of the wide scope of surgical resection, removal of the anal sphincter and removal of the rectal mesenteric draining lymph nodes to reduce the recurrence rate. However, in recent decades, LE has been favored by many surgeons. Compared with APR, this technique maintains patient quality of life due to its ability to avoid colostomy, and there is no difference in the recurrence rate. Surgical resection is the best option for such patients, especially in the absence of local and lymph node metastases. The goal of surgical resection is to achieve negative margins. This goal may be influenced by tumor size, anatomical location, degree of functional preservation and patient wishes. Although several studies have suggested that APR improves local recurrence rates compared to LE, other studies have not found a difference in local recurrence rates. Therefore, APR is not recommended as a treatment for anal melanoma in the absence of any demonstrable survival benefit and when it is technically feasible.

In this case, EUS revealed that the lesions were located in the mucosa and submucosa and did not invade the muscle layer. Because the lesion was far from the anus, the patient underwent extensive LE and lymph node dissection to ensure good postoperative quality of life. No local lymph node metastasis was found on postoperative pathology, which indicated stage I disease. The patient received temozolomide combined with cisplatin adjuvant chemotherapy. There is currently no optimal follow-up strategy for patients with mucosal melanoma. A retrospective study that analyzed the recurrence patterns of localized melanoma showed recurrence rates of 40%, 34%, 33%, 18%, and 0% at 1, 2, 3, 5, and 10 years, respectively. This finding is consistent with the recommended follow-up time for patients with cutaneous.
melanoma. Therefore, it is necessary to follow such patients for 5-10 years.

CONCLUSION

In summary, although the diagnosis of rectal mucosal melanoma remains difficult, EUS has a diagnostic role in identifying the depth of infiltration and provides a basis for surgical treatment modalities. Early diagnosis and appropriate management are necessary to improve the prognosis of rectal mucosal melanoma patients.

FOOTNOTES

Author contributions: Wei XX and Wang L contributed to manuscript writing and editing, and data collection; Xiong ZE, Xia C, Li ZY, Long C and Peng B contributed to patient management and histological evaluation; Wang T contributed to conceptualization and supervision; Xiong ZE and Wei XX contributed equally to this work as co-first authors. All authors contributed to revision for important intellectual content and approved the final version of the manuscript.

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