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Anorectal Melanoma: Radiologic-Pathologic Correlation

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Abstract: *Anorectal melanoma is a rare but aggressive disease. Because the patients often present with non-specific complaints, a high clinical suspicion is important to avoid a delayed diagnosis. It typically presents in the seventh or eighth decade of life with non-specific complaints such as rectal bleeding or anal pain. A timely diagnosis of anal melanoma is made even more difficult by the fact that most of the lesions lack obvious pigmentation and are even histologically amelanotic. Prognosis is very poor. Anorectal malignant melanomas spread along submucosal planes and are often beyond complete resection at the time of diagnosis. We present the radiological and pathological features seen in the three cases diagnosed with melanoma of rectum.*
Key words*: Anorectal melanoma, Imaging, Wide local excision, Abdominoperineal resection, Chemotherapy.*

I. Introduction

Anorectal melanoma is a rare but aggressive disease.[1] It is difficult to diagnose clinically, due to the non-specific symptoms and because it shows as a non-pigmented lesion in one third of cases.[1] Prognosis is very poor with a median survival of 24months and a 5-year survival of 10-15%.[9,12] Presently, there is no consensus on which surgical approach is favorable.[6] Anorectal malignant melanomas spread along submucosal planes, therefore, they are often beyond complete resection at the time of diagnosis.[13]

II. Epidemiology

The incidence of Anorectal melanoma has been doubled in the last 20 years with 1-2 cases per 1000000 populations in western countries.[1,2] Anorectal melanoma constitutes less than 1% (0.1%-4.6%) of all anorectal malignancies and less than 1%-2% of entire melanomas.[1,4-6]90% of melanomas reside in the skin; the remaining 10% is split between ocular melanoma (5%), melanoma of unknown origin (2%), and mucosal melanoma (3%). Among these, Anorectal melanoma is the third most common site, after the head/neck and the female genital system[2]. However, among primary melanomas residing in the gastrointestinal tract, the anorectal location is the most common.[7] Anorectal melanoma has female predominance, with 1.5:1 female to male ratio[1,4,6], although some authors claim that this small increase results from perineal scans being more common among females[6]. This disease usually affects elderly patients.

III. Clinical Symptoms

Anorectal melanoma presents with symptoms perfectly attributable to benign and much more common anorectal entities: rectal bleeding is the most common symptom, present in 53%-96% of patients, followed by the presence of a lump or mass, tenesmus, and more sporadically, itching, change in bowel habits or proctalgia.[1,4,5,7] Associated symptoms, of banal appearance, will continue for an average of 3-8 months until the final diagnosis, and entails a misdiagnosis rate close to 55%.[4] Anatomically, the majority of anorectal melanomas are located in the anal canal or in the dentate line. Only 2%-5% reside exclusively in the rectal mucosa.[4] Usually, they are tumors (pigmented or otherwise) of 2.9-3.8 cm in diameter[3] with an ulcerated, flat or polypoid appearance. A pigmented and polypoid lesion can be easily mistaken for a thrombosed hemorrhoid. Indeed, in an extensive review of the Memorial Sloan-Kettering Cancer Center (MSKCC), 8% of Anorectal melanoma diagnoses were performed after pathologic examination of hemorrhoidectomy parts; therefore, it is recommended to systematically analyze all resected specimens and send them, identified topographically, to the pathologist.[7,8]

Case histories

Case 1

A 79-year-old male presented with a 5-month history of a painful mass protruding from the anus with bleeding from the rectum and alteration of bowel habit. His medical history was unremarkable. A digital rectal examination revealed a hemorrhagic, soft mass of rectum.

Radiological Features

A computed tomographic scan of the pelvis revealed irregular thickening of the rectal wall, soft tissue mass arising from the rectal mucosa in the lumen. The mass showed moderate enhancement and homogeneity on contrast-enhanced CT scan image (Fig.1A, Fig.1B, Fig.1C).

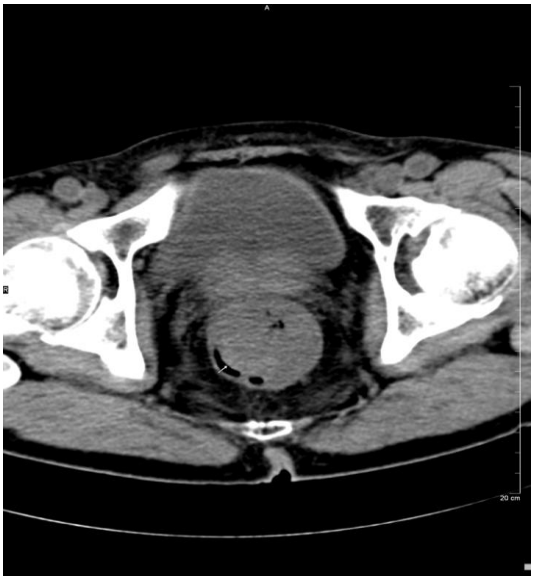

Fig.1A.Case1: Plain CT scan imageof the pelvis showing a soft tissue mass arising from the rectal mucosa in the lumen (white solid arrow).

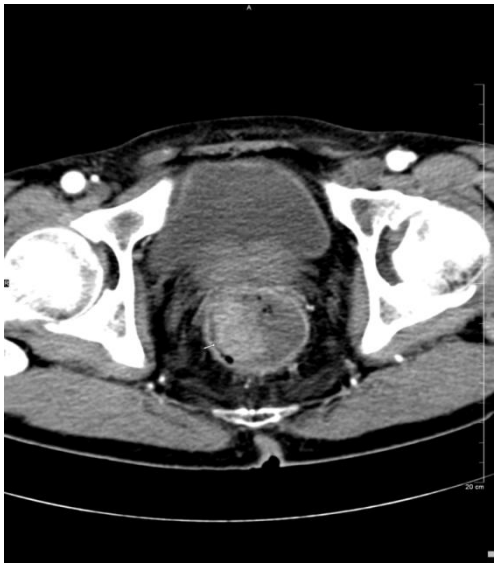

Fig.1B.Case1: Contrast-enhanced CT scan image of pelvis showing the soft tissue mass moderate enhancement and homogeneity (white solid arrow).

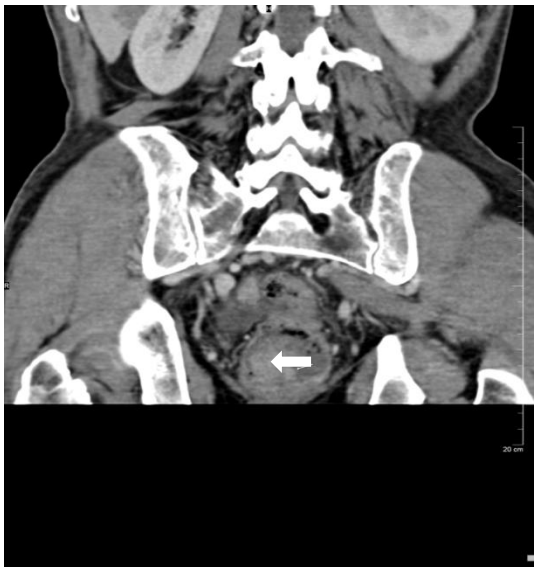

Fig.1C.Case1:Contrast-enhanced coronal CT scan image of pelvis showing the soft tissue mass connecting with rectal mucosa (white solid arrow).

Pathological Features

Microscopic evaluation of the tumoral biopsy fragments showed a high-grade, necrotic malignant tumor with scant vital tissue (Fig.1D). Areas with preserved architectural and cytologic details featured malignant epithelioid tumors growing in solid sheaths, with irregular polygonal nuclei and glassy cytoplasm. Immuno-histochemical examination showed tumor cells positive for S100, HMB45 and Melan-A.

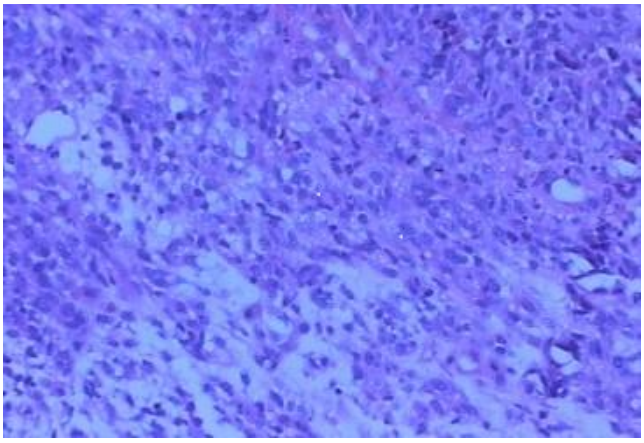

Fig.1D.Case1: Fragments of rectal mass showing coagulative necrosis and scant fragments of viable tissue, including shreds of tumor cells and a few mucous glands.

Case 2

A 61-year-old female presented with a 2-month history of bleeding from the rectum and alteration of bowel habit. She was a hypertensive patient under medication. A digital rectal examination revealed a hemorrhagic, soft mass of rectum.

Radiological Features

A computed tomographic scan of the pelvis revealed local irregular thickening of the rectal wall, findings consistent with colorectal cancer and a small node arising from rectal mucosa. The node showed moderate enhancement on contrast-enhanced CT scan image (Fig.2A, Fig.2B, Fig.2C).

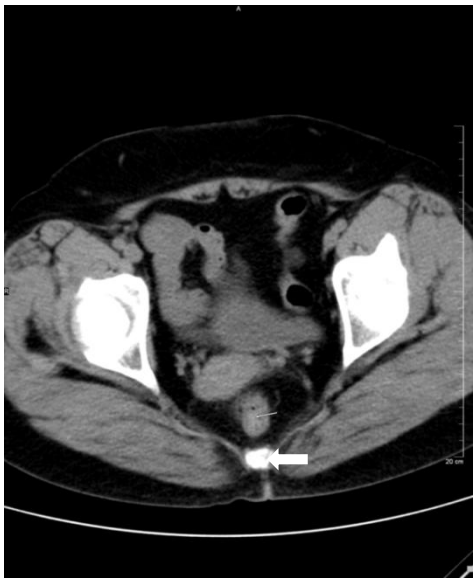

Fig.2A.Case2: Plain CT scan image of the pelvis showing a small node arising from the rectal mucosa (white solid arrow).

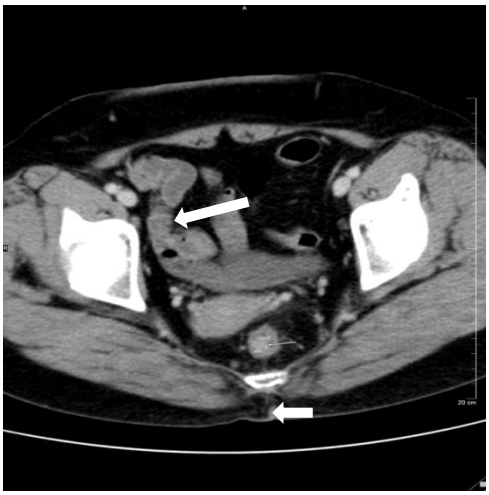

Fig.2B.Case2: Contrast-enhanced CT scan image of the pelvis showing the node moderate enhancement (white solid arrow).

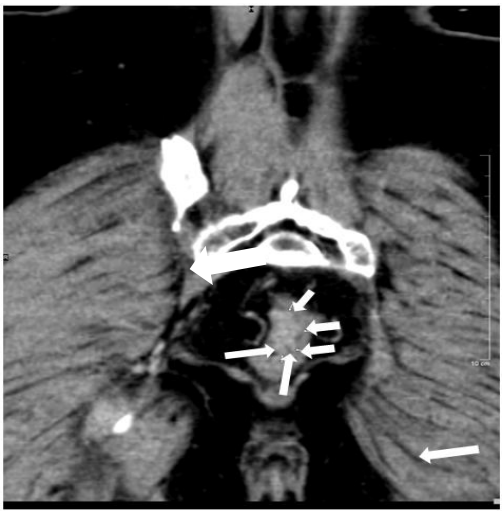

Fig.2C.Case2: Contrast-enhanced coronal CT scan image of the pelvis showing the node connecting with rectal mucosa (white solid arrows).

Pathological Features

Microscopic evaluation of thetumoral biopsy fragments revealed pleomorphic lesions displaying high mitotic rate and prominent nucleoli. It showed intra- and extra-cellular melanin pigment on microscopic examination (Fig.2D).

Immuno-histochemical examination showed tumor cells positive for S100, HMB45 and Melan-A.

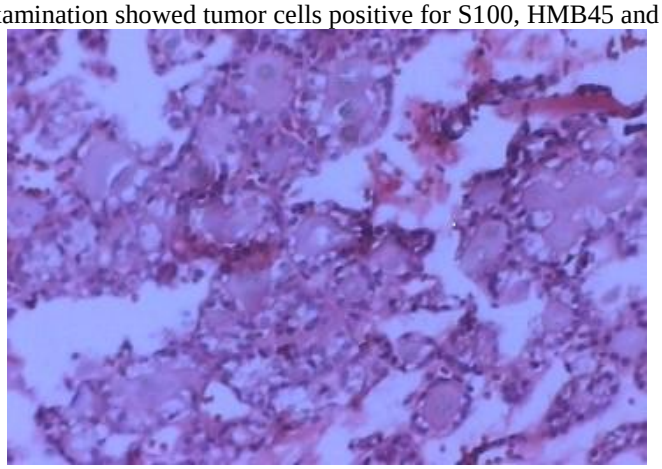

Fig.2D.Case2: Histopathological biopsy sample shows pleomorphic lesions with melanin pigment.

Case 3

A 74-year-old female presented with a 4-month history of bleeding from the rectum and alteration of bowel habit. She was non-smoker with unremarkable medical history. A digital rectal examination revealed a hemorrhagic soft mass of rectum.

Radiological Features

A computed tomographic scan of the pelvis revealed partial bowel wall thickening and dilatation of intestine at the sigmoid colon with small lymph nodes around and abdominal aortic wall calcification (Fig.3A, Fig.3B, Fig.3C).

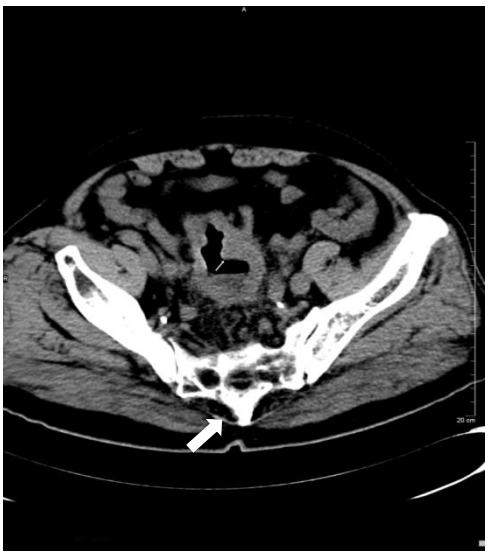

Fig.3A.case3: Plain CT scan image of the pelvis showing partial bowel wall thickening and dilatation of intestine at the sigmoid colon (white solid arrow) with small lymph nodes around.

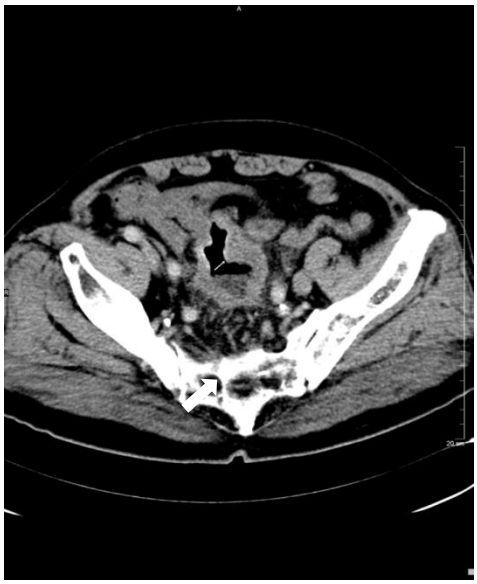

Fig.3B.case3: Contrast-enhanced CT scan image of the pelvis showing the tumor slightly enhanced homogenously (white solid arrow).

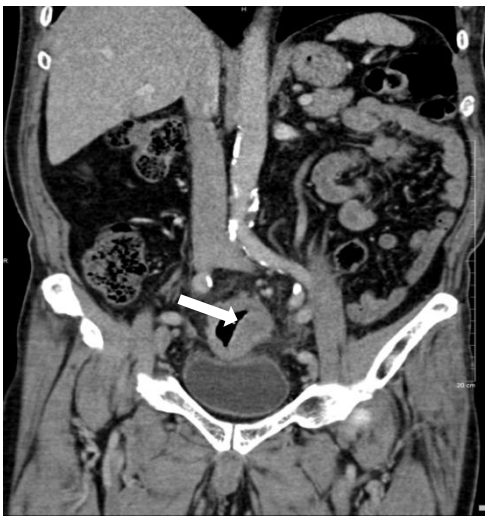

Fig.3C.case3: Contrast-enhanced coronal CT scan image of the pelvis showing partial bowel wall thickening and dilatation of intestine at the sigmoid colon (white solid arrow).

Pathological Features

Histopathological biopsy sample of the rectal mass showed atypical polygonal cells with frequent mitotic figures (Fig.3D). Areas of coagulative necrosis were common.

Immuno-histochemical examination showed tumor cells positive for S100, HMB45 and Melan-A.

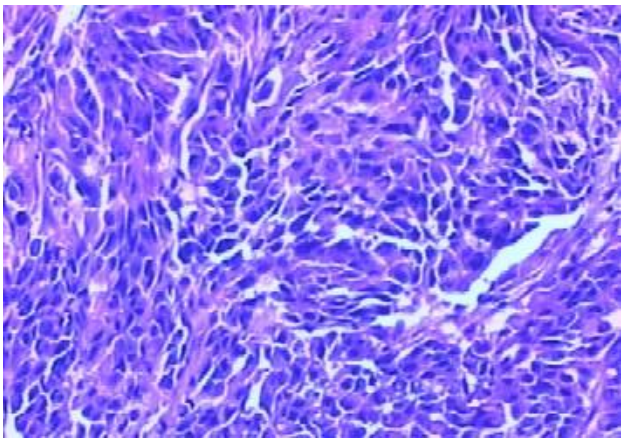

Fig.3D.case3: Biopsy sample of the rectal mass showing atypical polygonal cells with stainable cytoplasm, hyperchromatic nuclei and smudged chromatin.

IV. Discussion

All melanomas, whether cutaneous or mucosal in origin, originate from melanocytes, which are cells derived from the embryological neural crest. During fetal development, these cells migrate to many sites throughout the body, primarily to the skin. However, melanocytes also reside in the eyes (retina and uveal tract) and mucosal surfaces.[6,10] Therefore, cutaneous melanomas are by far the most common form of the disease, comprising more than 90% of all melanomas. Of the remaining 10% forms of melanoma, ocular melanoma accounts for 5%, melanoma of unknown origin for 2%, and mucosal melanoma for 3%. Melanocytes may undergo malignant transformation when exposed to ultraviolet UVB light, which is a carcinogenic stimulus.

However, this relationship is not apparent in anorectal melanoma.[13] There is a likely role of immunology in the development of anorectal melanoma as the incidence is higher in patients with Human Papilloma virus (HPV) and Human Immunodeficiency virus (HIV) infections.[13,14] In the rectum, melanocytes are located at the anal transition zone and squamous zone. Most anorectal melanomas arise from the dentate line and 65% are located within the anal canal or at the anal verge.[6,13] The most common presenting complaints are bleeding, anorectal discomfort or pain, an appreciable anorectal mass, or change in bowel habits. Other symptoms include pruritis, tenesmus, prolapsed hemorrhoid, change in stool habits, and diarrhea. Patients who have metastasis at the time of presentation may additionally have fatique, weight loss, and anemia.[6,13] Lesions are most commonly found at the anorectum, followed by the anal canal and anal verge.[11] These lesions are often discounted as being benign hemorrhoids or polyps.[12,13]

A sigmoido-colonoscopy is essential both for evaluation of the cause of symptoms and obtaining a tissue biopsy from a suspicious lesion. Endoscopic endorectal ultrasound may be considered to evaluate tumor thickness and surrounding nodal status.[13]

Computed tomography (CT) scan of the abdomen and pelvis is not the preferred diagnostic modality to evaluate hematochezia or alteration in bowel habit, but is a valuable tool to assess regional disease, and is frequently utilized to determine if there is lymphadenopathy or metastasis once neoplasia is suspected.[10,12,13] Contrast-enhanced CT scan and MRI allow characterization and assessment of the extent of the tumor. On CT scans, primary rectal malignant melanomas appear as bulky intraluminal fungating masses in the distal rectum, focally expanding and obscuring the lumen without causing obstruction, with perirectal infiltration and frequently enlarged lymph nodes.[15] Rectal carcinoma or other rectal masses present as significant obstruction. In our cases, irregular thickening of the rectal wall was the common CT finding.

MRI shows the melanotic component as high signal intensity on T1-weighted imaging and mixed signal intensity on T2-weighted imaging.[16]Extraluminal extent of the lesion is better demonstrated by MRI imaging. Other rectal mass lesions show hypointense signal on T1-weighted imaging.

In cases of diagnostic difficulty, which is frequent even on histopathology, the presence of melanin can be helpful, but it is not easily detected in anorectal disease.[13]In our cases, presence of melanin was a diagnostic marker. Melanoma antigens S-100, HMB-45, and vimentin are important immuno-histochemical markers. In our cases, immuno-histochemical examination showed tumor cells positive for S100, HMB45 and Melan-A. Polyclonal antiserum and monoclonal antibodies to carcinoembryonic antigen can help to distinguish it from a poorly differentiated epidermoid carcinoma.[10,13] Activating KIT-gene mutations, which are implicated in leukemia and gastrointestinal stromal tumors have been associated with the pathogenesis of malignant melanoma.[6]

Malignant melanoma of the rectum is a rare and very aggressive rectal tumor.[9] Lymphatic spread to the inguinal or inferior mesenteric node is common. The most common sites for metastases are inguinal lymph

nodes, mesenteric lymph nodes, hypogastric lymph nodes, para-aortic lymph nodes, liver, lung, skin and brain.[10] The incidence rates for locoregional lymph node metastases on initial presentation are almost 60%.[9,10] At the time of diagnosis, distant metastases are identified in 26-38% of patients.[6,10]

Anal melanoma is staged on a clinical basis, focusing on loco-regional and distant spread. Stage I is local disease only, Stage II is a local disease with increased thickness and ulcerations, Stage III is local disease with involvement of regional lymph nodes, and Stage IV shows distant metastatic disease.[10,13]

The treatment of anal melanoma, unfortunately, is only moderately successful. Surgery remains the cornerstone of treatment.[9,10] Of all patients diagnosed with anorectal melanoma the 5-year survival rate can range from 16 to 34%. In patients who have metastasis at the time of diagnosis, the disease-free survival rate may drop to 16% from 22%.[6,13] The controversy has been whether abdominoperineal resection (APR) is needed or wide local excision (WLE) is adequate for complete treatment. APR, although a highly morbid operation, has long been thought to be the best means of control of anorectal melanoma. Lately, there has been a paradigm shift after several studies indicated that WLE may be adequate to control disease, while minimizing the morbidity of surgery because anorectal melanoma is a systemic disease at the time of diagnosis and no surgical treatment, regardless of how aggressive, will truly change the outcome.[6,9,10,13] The benefits of a WLE are quicker recovery, no need for a stoma, and minimal impact on bowel function.[13] Lymph node dissection may be indicated in clinically apparent disease or for occult disease identified with sentinel lymph node (SLN) techniques.[6,10]

There are no standards regarding systemic therapy for disseminated disease. Chemotherapy, radiation therapy, and immune therapy have a limited role. The medications used in adjuvant therapy are cisplatin, vinblastine, dacarbazine, interferon B, and Interleukins IL-2-8. Dacarbazine is the most commonly used single agent and usually initiates a partial response in 20% of patients in 4-6 months after treatment.[10,13] Recent studies show that wide local excision (WLE) combined with adjuvant loco-regional radiotherapy result in comparable loco-regional control with less loss of function compared to APR.[9]

The rarity of this disease and the limited number of patients who present with early disease, have prevented definitive trials examining the optimal treatment of curable anal melanoma.[6,10,12,13]

V. Conclusion

Anorectal melanoma is extremely rare, highly aggressive, and difficult to diagnose. Bulky fungating masses in the distal rectum obscuring the lumen without causing significant obstruction seen on CT and MRI scans raise the possibility of anorectal malignant melanoma. On MRI, the melanotic component of rectal mass can be seen as high-signal intensity on T1-weighted imaging further strengthening the diagnosis. Although biopsy and histopathological examination are essential for diagnosis, distinct radiological features on CT, and MRI may suggest the possibility of malignant melanoma. Major role of CT and MRI is in preoperative staging of the tumor.

Although surgery remains the cornerstone of treatment, the exact procedure remains controversial. Role of adjuvant therapies is minimal. The delayed diagnosis of anorectal mucosal melanoma (ARMM) leaves a poor prognosis and a standardized evidence-based treatment approach is not well-defined due to the rarity of this disease.[17]

The only hope of improved survival lies in early diagnosis and treatment. Since, the complaints are usually non-specific; this is only possible with a high index of suspicion followed by early sigmoidoscopy and biopsy.

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