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Abstract
Malignant melanoma of the anorectum is a rare but highly aggressive tumor. We report our experience of anorectal melanoma in five patients. Of these, two have advanced disease, two had localized disease and one patient had florid systemic metastases with a history of hemorrhoidectomy one year prior. One patient whose metastatic workup was negative, expired on post–op day 15 of abdominoperineal resection due to unsuspected but florid cerebral metastases. Another patient with localized disease underwent an APR with curative resection and post–op whole body PET scan negative for occult or residual disease. Advanced stage patients were referred for chemotherapy. To improve prognosis, it is important to detect anorectal melanoma at an early stage.

Keywords
anorectum, melanoma, malignant

Introduction
Malignant melanoma is a rare and very aggressive tumor of anal canal and rectum. The anorectum is the third most common location of malignant melanoma after the skin and retina accounting for 1–2 % of all malignancies in this location. Only 500 cases have been reported so far. The possibility of skip lesions and occult metastases, which may commonly be unpredictable, is invariably the cause of poor outcomes despite aggressive multimodal therapy. At the time of presentation, 20% of patients have regional and 40% have distant metastases. Metastasis to nodes, lungs, liver, bone and brain are known to occur. Mucosal melanomas generally have a poor prognosis. Treatment options are ambiguous due to paucity of clinical trials. For a localized disease, opinions vary from aggressive approach to local therapies, but the outcome remains dismal despite multimodal therapy. Adjuvant radiation may decrease locoregional recurrence but overall survival remains poor. We report a case series of five patients of anorectal MM.

Case Series
Case 1
A 50–year–old female presented to orthopedician with increasing pain and swelling in her left upper leg of one month duration. On examination, there was a smooth, firm, fixed and tender swelling measuring 3x3 cm in lateral aspect of her right upper leg (Figure 1). The overlying skin was normal. X–Ray of the leg showed a lytic lesion in fibula. The patient was referred to the Department of Pathology with a request for FNAC from
Case 2

A 45-year-old male was found to harbor multiple liver metastases on routine USG abdomen for non-specific abdominal complaints. A USG guided percutaneous FNAC was suggestive of malignant melanoma. A thorough search for primary tumor site including subungual and intertrigal regions yielded no result. A detailed inquiry from the patient revealed a history of hemorrhoidectomy a year back. A proctoscopic examination showed a melanotic papule on the anterior wall of rectum 7 cm from anal verge about 1 cm in size. Excision biopsy confirmed it as the primary site of malignancy. Patient was referred to medical oncologist in view of disseminated disease. Ironically and unfortunately, the biopsy report of excised hemorrhoids was suggestive of malignant melanoma, but was never looked up until a year later.

Case 3

A 59-year-old male presented to surgical OPD with complaints of intermittent rectal bleeding and prolapse mass per rectum for 5 months. On examination, a pigmented growth on anal verge at 4–7 o’clock extending into anal canal for up to 2 cm was seen. Surrounding induration was present but luminal narrowing was not there. Sphincters appeared involved. Punch biopsy showed Malignant Melanoma of the anal canal. Metastatic workup (CECT chest, abdomen and pelvis with serum biochemistry) was negative for any distant metastases. APR with end colostomy was done. Immediate postop period was uneventful but on POD5 patient became delirious. Metabolic workup was normal. MR brain showed multiple brain metastases. Patient was managed supportively but expired on POD 15.

Case 4

A 55-year-old female presented to surgical OPD with complaints of protrusion of mass from anus for 6 months which was gradually increased in size and recently became painful. There was no history of constipation. O/E grossly infiltrating growth per annum with luminal compromise precluding digital rectal examination was seen. On PV examination, 7 cm long growth was felt in the anterior wall of rectum through the posterior wall of vagina. Vaginal mucosa was mobile. Punch biopsy from the growth was suggestive of malignant melanoma. Diversion colostomy was offered in view of advanced nature of disease with featured of partial large bowel obstruction and patient was referred for palliative chemotherapy.
A 55-year old male presented to surgical emergency with complaints of colicky lower abdominal pain, loss of appetite and bleeding per rectum for 6 months. The anal canal was normal on inspection and palpation. On digital rectal examination, the sphincter tone was normal. An extraluminal swelling was noted in the posterior rectal wall with partial compromise of the lumen. The overlying mucosa was normal. Proctoscopy confirmed the extraluminal nature of the lump. A core cut biopsy was suggestive of malignant melanoma. CECT pelvis showed a retro rectal lump with no evidence of local infiltration. CECT chest–abdomen and whole body PET scan showed no evidence of distant metastases. The patient was counselled and an APR with end sigmoidostomy was done. The patient is doing well at six months of follow-up.

**Discussion**

Anorectal melanoma is a rare malignancy accounting for only 1–2% of anorectal tumors. The anorectum is the third most common location of malignant melanoma after the skin and retina. Malignant melanomas occur frequently in the anorectum because of the presence of abundant melanocytes in the mucosa of the anal canal. The metastases are highly unpredictable and skip lesions are possible. Up to 20% patients have regional disease at presentation and 40% present with distant metastasis to nodes, lung, liver, bone and brain. The absence of early clinical manifestations and the lack of clinical suspicion contributes for delayed diagnosis. Owing to its rarity and histologic variability, misdiagnosis as lymphoma, carcinoma, or sarcoma is common. Histopathological examination and immunohistochemical studies are of great importance in the diagnosis of anorectal MM. Positive protein S–100, melanoma antigen HMB–45, and melan–A expression strongly support the diagnosis of melanoma. Anti–S–100 protein is the most common screening immunohistochemical stain used in the diagnosis of malignant melanoma and is highly sensitive for melanocytic differentiation. The main determinants of prognosis are the depth of invasion and stage of the disease. The factors for poor prognosis include advanced disease at the time of diagnosis and rich vascularity which increases the risk of hematogenous metastasis. Abdomino–perineal resection (APR) is the treatment of choice for patients with <2 mm wide lesion. Radiotherapy is palliative in locally extensive tumors while combined with chemotherapy is used for metastasis. Chemotherapy is generally used for palliative purposes in advanced stages of MM and survival after diagnosis is quite short. There are standard systematic treatment options defined in advanced cutaneous MM patients, including cisplatin, vinblastine, DTIC, IFN,
and interleukin–2. Because of the limited number of studies, there is no standard treatment for mucosal MM. Another alternative is an orally bioavailable drug, temozolomide. Yeh et al. used a combination regimen with cisplatin as the third line of treatment after colostomy and radiotherapy, TMZ, and liposomal doxorubicin for a 49-year-old female anal mucosal melanoma patient with complete colonic obstruction and multiple distant organ metastases. After the second course, more than 50% regression was observed in the metastases in all regions. Ipilimumab, which is an immunomodulatory monoclonal antibody, was developed against an antigen on T lymphocytes. Common T lymphocyte antigen–4, an antigen that is related to cytotoxic T lymphocytes, has a pressurizing function on cytotoxic T cells. Blocking this antigen results in cytotoxic T cells movement against cancer cells. Ipilimumab is accepted as an alternative treatment option for patients with resistant cutaneous MM, but its place in primary anorectal MM treatment should be further studied. Incorporation of immunotherapy in the management may improve outcome. The prognosis is very poor, with less than 20% survival five years after diagnosis.

**Conclusion**

Anorectal malignant melanoma is a highly lethal disease of elderly people, which often manifests with advanced disease. There can be considerable histologic variability, and the use of a panel of immunohistochemical stains, including S-100 protein, Melan A, HMB-45, tyrosinase, and a pankeratin, is helpful to the diagnosis. Clinicians should suspect anorectal melanoma in cases presenting with blood in the stool. Furthermore, the prognosis depends on the staging, and it is important to detect anorectal melanoma at an early stage. Presently, advanced anorectal MM remains an incurable disease, and despite the use of multidisciplinary strategies (radical surgery, immunotherapy, chemotherapy, and radiotherapy), it remains a fatal disease.

**References**