Section: General Surgery

Case Series

ANO-RECTAL MALIGNANT MELANOMA: A CASE SERIES

Rinki Das[1], Ritankar Sengupta[2], Doyel Halder[3], Saurabh Das[1], Tanup Das[4], Sourav Chatterjee[4], Jayanta Halder[4], Asim Kumar Manna[5]

[1]Associate Professor, Department of General Surgery, IPGME & R, Kolkata, West Bengal, India.
[2]Associate Professor, Department of General Surgery, Deben Mahata Government Medical College, Purilia, West Bengal, India.
[3]Demonstrator, Department of Pathology, IPGME&R, Kolkata, West Bengal, India.
[4]Junior Resident, Department of General Surgery, IPGME&R, Kolkata, West Bengal, India.
[5]Professor, Department of Pathology, IPGME&R, Kolkata, West Bengal, India.

Received : 07/08/2025
Received in revised form : 22/09/2025
Accepted : 10/10/2025

Keywords:
Malignant melanoma, anorectal malignant melanoma, mucosal melanoma, metastatic melanoma, syndromic melanoma

Corresponding Author:
Dr. Rinki Das,
Email: rinkid123@gmail.com

DOI: 10.47009/jamp.2025.7.5.248

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (5); 1301-1306

ABSTRACT

Background: Anorectal melanoma is a rare and aggressive malignancy of the anal canal and distal rectum which may occasionally manifest as a familial or part of a syndromic presentation. Due to its non-specific symptoms such as anal bleeding, anal mass or pain pre-operative clinical diagnosis remains difficult particularly if the lesions are devoid of clinically evident melanin pigments. Surgical resection remains the mainstay of treatment. The optimal surgical procedure for primary tumours is controversial and can vary from wide local excision to an abdomino-perineal excision of the rectum (APR) and anal canal or more aggressive surgery requiring inguino-pelvic lymphadenectomy depending on the presentation. For locally advanced and metastatic disease systemic chemotherapy has limited advantages. Novel immune check point inhibitors have some role in achieving improved survival particularly in advanced cases. **Materials and Methods:** We present a prospective analysis of seven patients with anorectal malignant melanoma. After a diagnosis of malignant melanoma was made on histopathological examination with or without immunohistochemistry staining patients were evaluated with triphasic contrast enhanced tomography of thorax, abdomen, and pelvis or with whole body ^{18}F-FDG PET-CT scan for clinical staging. The patients were subjected to various modes of treatment such as local resection, or abdominopelvic excision of rectum (APR) or palliative therapy depending on their presentations and were followed to study the survival. **Result:** Median age at presentation was 48 years, five patients presented with loco-regional disease and two patients presented with metastatic disease. One of the patient with metastatic disease had syndromic presentation with multiple first and second order relatives with neurofibromatosis type 1. Two patients were treated with local excision, three patients underwent abdomino-perineal excision of rectum and one patient underwent additional pelvic lymphadenectomy along with abdominoperineal excision of rectum. Patients in stage III and one patient with stage IV disease received systemic therapy with Dacarbazine. One patient with liver metastasis is planned for immunotherapy after local excision of the bleeding anal mass. Mean survival in our series was 22 ± 4.9 months for patients with Stage I-III disease. **Conclusions:** Anorectal melanoma is a rare and aggressive malignancy. Patients usually present with advanced disease and surgical therapy includes wide local excision to more aggressive procedures such as abdomino perineal excision of rectum with or without pelvic and inguinal lymphadenectomy. Adjuvant combined chemotherapy has limited role in prolonging survival. Immune-checkpoint inhibitors especially in metastatic scenario remain important therapeutic options for these patients.

INTRODUCTION

Melanoma of the anal canal is a rare form of malignancy. Its incidence is 2.7 per 10 million populations per year and it consists of 0.05% of cases of ano-rectal malignancies.[1-3] Familial or hereditary cases of malignant melanoma have exhibited underlying genetic abnormalities of most commonly

the CDKN2A and CDK4 genes (familial atypical multiple mole melanoma syndrome).[4] Malignant melanomas may also develop in patients with neurocutaneous syndromes particularly Neurofibromatosis type 1 and type 2, ataxia telangiectasia, xeroderma pigmentosa and are often associated with tumours of the nervous system including astrocytoma, medulloblastoma, glioblastoma multiforme, ependymoma, glioma, meningioma, and acoustic neurilemmomas. Germline variants in TERT, MITF, and BAP1 are also known to predispose cutaneous and mucosal melanomas.[4] Malignant melanoma of the anal canal is more frequently observed in female gender The median age at presentation is in the sixth decade of life. Contrary to the pathogenesis of cutaneous melanomas primary anal canal melanomas do not have any definite risk factors. Anorectal melanomas usually present in an advanced stage.[5] The clinical features are similar to other anal canal cancers which include perianal mass lesion, tenesmus, anal incontinence, bleeding and enlarged inguinal lymph nodes. 30%-40% cases present with metastases at distant organs of which liver and lungs and brain are the commonest sites.[6] Approximately 20-30% cases are without pigmentation i.e. amelanotic and require immunohistochemistry staining for S-100, Melan A, tyrosinase and HMB 45 for its diagnosis.[7-10]

T staging of rectal and anal canal melanoma differ in terms of rectal wall involvement versus tumour size for tumours of the anal canal. Staging of anal canal tumors is as follows: Stage I: tumour size <2 cm without lymph nodal involvement or distant metastates, Stage II: tumour size > 2 cm without lymph nodal involvement or distant metastates, stage III: tumour invading adjacent organ or tumour with loco-regional lymphadenopathy, stage IV: presence of distant metastasis.

Staging of rectal melanoma Stage I: tumour limited to muscularis propria without lymph nodal involvement or distant metastates, Stage II: tumour invading perirectal tissue or other adjacent organs without lymph nodal involvement or distant metastates, Stage III: tumour with loco-regional lymphadenopathy, stage IV: presence of distant metastasis.[11]

Treatment varies from wide local excision, to endoscopic mucosal resection, to an abdomino-perineal excision of rectum with or without pelvic and inguinal lymohadenectomy depending on the presentation. For anorectal melanoma survival after APR or local resection are similar.[12-14]

Male gender, depth of infiltration, tumour necrosis, perineural invasion, amelanotic subtype, lymph nodal metastasis, and distant metastasis are associated with poor overall survival.[12]

Regarding adjuvant systemic therapies traditional chemotherapy with Dacarbazine or Temozolomide is associated with a 20% survival. Patients with c-KIT mutation may be treated with Sorafenib or Imatinib. In a metastatic scenario immunotherapy seems to have some effects on prolongation of survival. Recently, immune check point inhibitors such as, nivolumab, pembrolizumab and ipilimumab are approved for treatment of melanomas.[15-16]

MATERIALS AND METHODS

We present a prospective analysis of seven patients presented with anorectal malignant melanoma at a tertiary center of West Bengal from 2017-2025. After a diagnosis of malignant melanoma was made on histopathological examination with or without immunohistochemistry staining patients were subjected to thorough clinical examination to rule out any cutaneous, oropharyngeal or genital melanotic lesions. Esophagoduodenoscopy, rhinopharyngoscopy, and ophthalmological examinations were also carried out to rule out any other site of origin. Full length colonoscopy was performed for all the cases to note the disease extent and to rule out other lesions. The patients were then evaluated with triphasic contrast enhanced tomography of thorax, abdomen, and pelvis or with whole body 18F-FDG PET-CT scan for clinical staging in select cases. The patients were subjected to various modes of treatment such as local resection, or abdominopelvic excision of rectum or palliative therapy depending on their presentations and were followed to study the survival.

RESULTS

We report the clinical presentation of seven cases, clinical stage at presentation, histopathological and immunohistochemistry findings and the treatment outcome. Five patients in our series were male and two were female. Median age at presentation was 48.5 years [range 42-64 years]. Four of them had the primary disease at the anal canal and the others had the lesions at the ano-rectal junction. Most frequent presentation was a perianal mass along with bleeding per rectum. One patient presented with right inguinal lymphadenopathy and on further imaging was identified with lung metastases. Two patients with pedunculated anal mas were treated with local excision. One of them had multiple bilobar liver metastasis and the other had disease confined to the anal canal only. Three patients underwent abdomino-pelvic excision of the rectum and one patient underwent additional pelvic lymphadenectomy. (Table 1). Histopathology findings were corroborative of malignant melanoma with presence of enlarged polymorphous cells with large vesicular nuclei, irregular nuclear borders, condensed chromatin, and numerous atypical mitoses along with dark-brown pigment clusters between the cells.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Case details

	Case-1	Case-2	Case-3	Case-4	Case-5	Case-6	Case-7
Age	64	48	42	55	45	52	45
Gender	M	M	F	F	M	M	M
Symptoms	Bleeding per rectum	Bleeding per rectum, inguinal lymphadenopathy	Perianal mass, bleeding	Perianal mass	Bleeding per rectum	Bleeding per rectum, Mass protruding from the anal canal	Bleeding per rectum, Mass protruding from the anal canal
Site of the primary lesion	Anorectal junction	Anal canal	Ano-rectal	Anal canal	Anal canal	Anorectal junction	Anal canal
Stage at presentation	III	IV	III	II	I	III	IV
If Stage IV, site of metastasis		Lungs	-				Liver
Syndromic / not	-	-	-	-	-	-	NF Type 1
Type of surgery	APR	Biopsy	APR with pelvic lymphadenectomy	Local excision	APR	APR	Local excision
Tumour thickness (mm)	13	-	14	9	10	12	12
Tumour diameter (cm)	3.5	2	3	4	3	7	10
Mural involvement	Perirectal soft tissue	-	Perirectal soft tissue	Mucosa	Muscularis propria	Perirectal soft tissue	Mucosa
Lymph node involvement	present	-	Present	-	-	present	-
Histology	mixed	mixed	Mixed	spindle	mixed	mixed	Mixed
LVI	present	-	Present	-	-	present	present
PNI	no	-	Present	-	-	present	-
Melanin	Present	present	Present	present	present	present	present
IHC Melan-A	-	positive	-	positive	positive	positive	Positive
IHC HMB-45	-	positive	-	positive	positive	positive	Positive
IHC S-100	-	positive	-	positive	positive	positive	positive
Systemic therapy	Dacarbazine	Dacarbazine	Dacarbazine (incomplete treatment)	-	-	Dacarbazine + Cisplatin	Planned for immunotherapy
RFS / PFS (months)	21	-	11	27	20	7	0.5
Site of recurrence	liver	-	Liver	-	-	-	-
Overall survival / end of follow up (months)	25	3	16	27	20	7	0.5

Patients in stage III and IV received systemic therapy with Dacarbazine. Mean survival in our series was 22 ± 4.9 months for patients with Stage I-III disease treated surgically. One stage IV patient is in his early postoperative period and the other survived for 3 months only. [Case details are presented in Table 1].

ISSN (O): 2687-5365; ISSN (P): 2753-6556

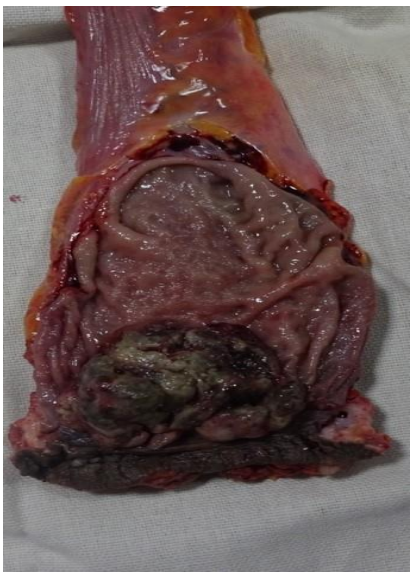


Image 1: Case-1 Cut open specimen of APR

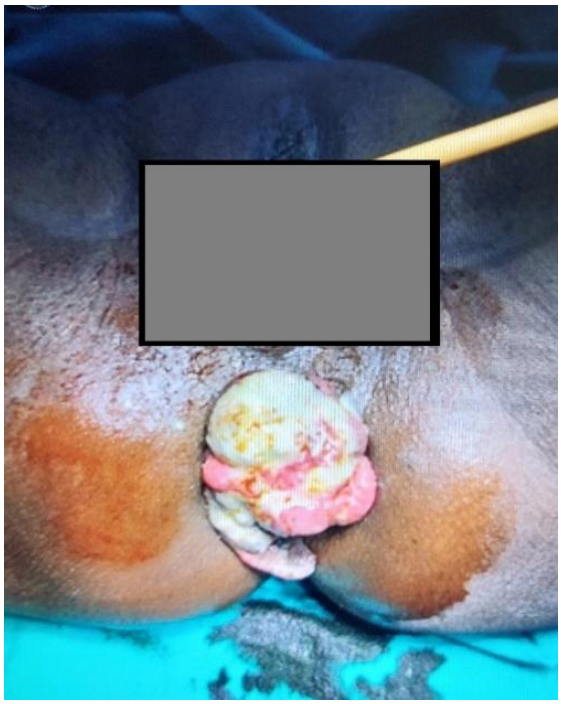


Image 2: Case-4, large mass arising from the anal canal with a narrow stalk, local exicision carried out

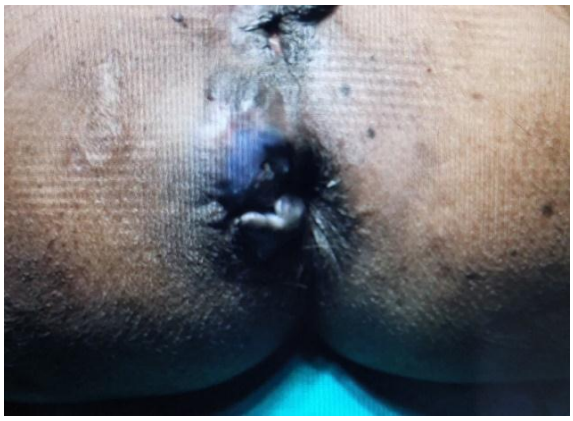


Image 3a: Case-3: perianal mass

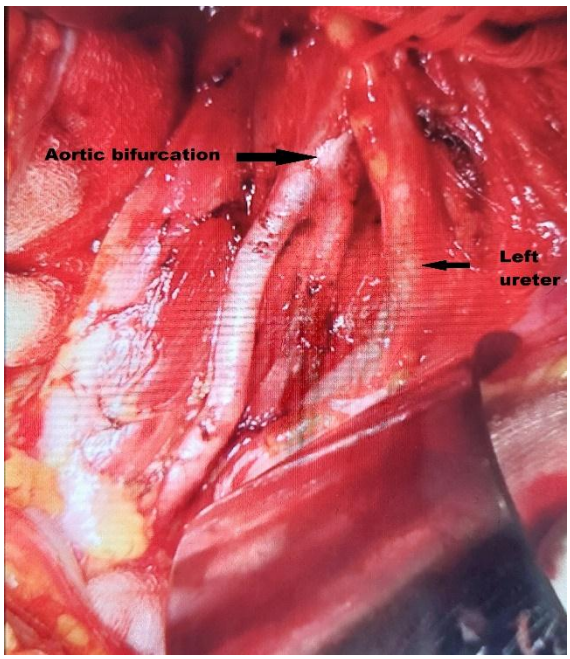


Image 3b: surgical field following pelvic lymphadenectomy

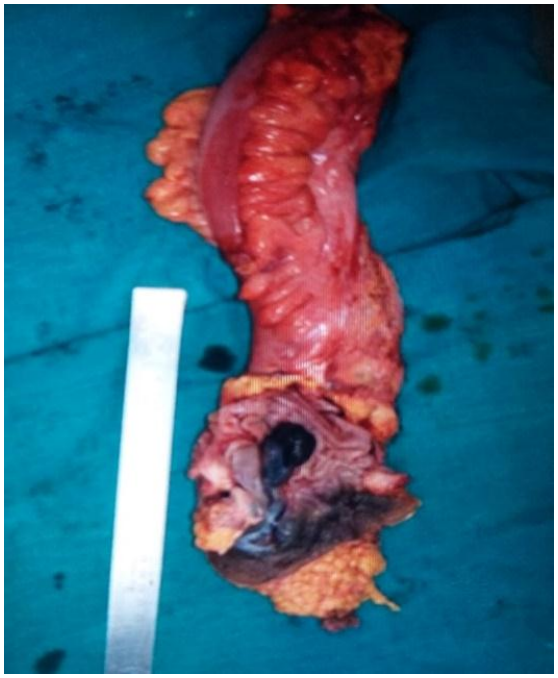
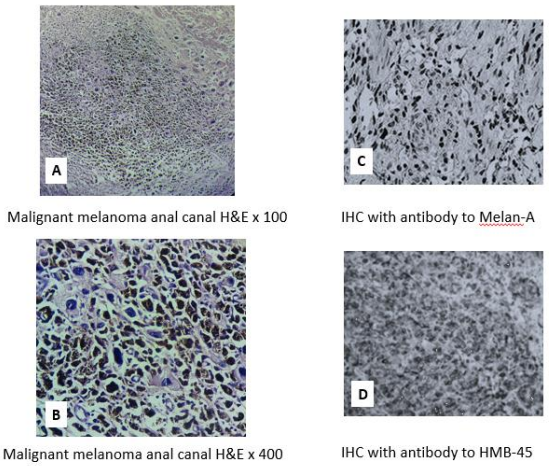


Image 3c: Case-3: Cut open specimen of APR showing the ano-rectal melanoma

ISSN (O): 2687-5365; ISSN (P): 2753-6556



Malignant melanoma anal canal H&E x 100 | IHC with antibody to Melan-A

Malignant melanoma anal canal H&E x 400 | IHC with antibody to HMB-45

Image 3d: Microphotographs of H& E and IHC for Melan A and HMB-45

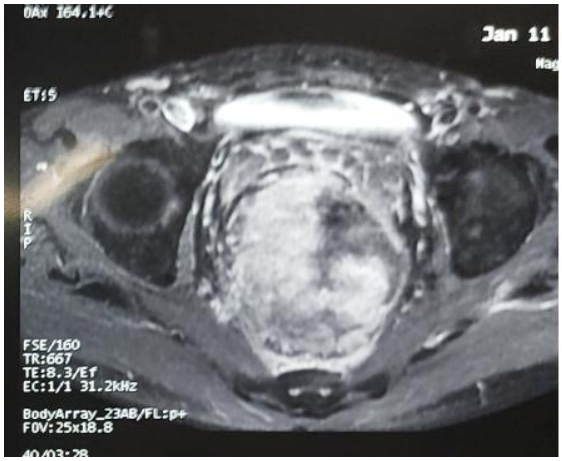


Image-4a: Case 6: MRI pelvis showing a large ulcero-proliferative mass in the mid and lower rectum, with near-complete occlusion of the lumen, T1 hypointense and T2 hyperintense lesion with diffusion restricted necrotic component and perirectal lymphadenopathy

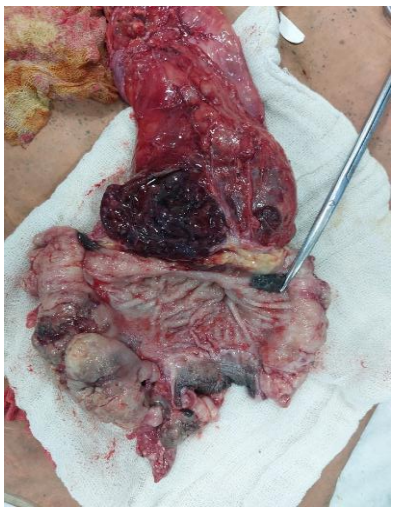


Image-4b: Case 6: Specimen of APR with large heterogeneous ulceroproloferative lesion in the ano-rectal junction and anal canal with small melanotic nodular region

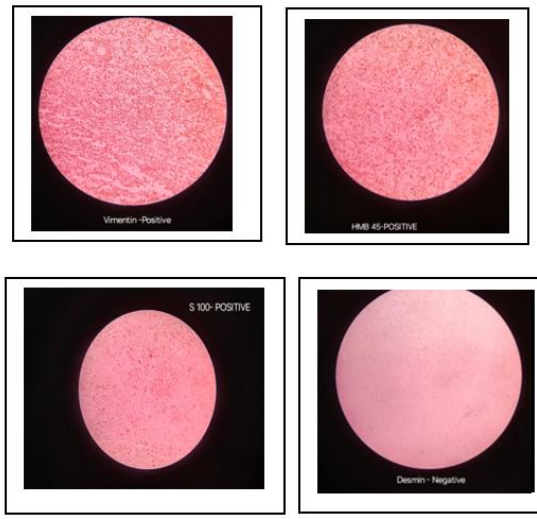


Image 4c: Case 6: IHC profile showing Vimentin positive, HMB-45 positive, S-100 positive, Desmin negative tumour

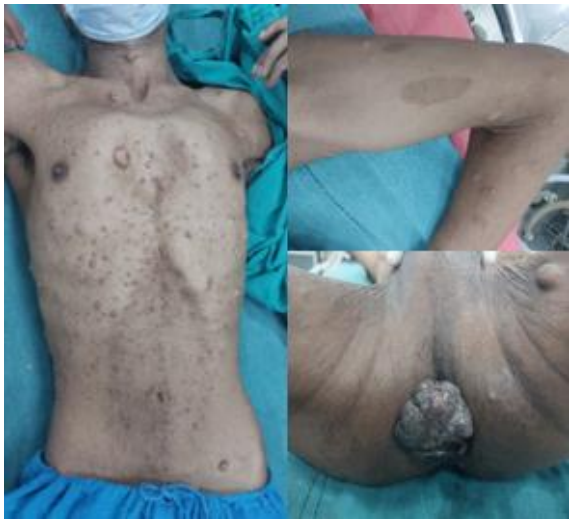


Image 5: Case 7: Multiple cutaneous nodules, Café-au-lait spots at the left leg and anal proliferative lesion in a case of neurofibromatosis-type 1

DISCUSSION

Anorectal malignant melanoma is a lethal condition, often present at a very advanced stage and the extent of optimum resection required for best survival is debated. Local excision is associated with less morbidity and similar rates of survival is observed in absence of any locoregional lymphadenopathy.[12] During APR, mesorectal lymph nodes are resected en bloc with the primary lesion. The need for regional lymphadenectomy for anorectal melanoma is still unclear. Inguinal, pelvic sidewall, and mesorectal lymph nodes are at risk for metastases from anorectal lesions. However, it is believed that the extent of resection is not associated with survival as systemic dissemination occurs very early in the disease and more than 75% cases with anorectal melanoma present with disease recurrence.[17-19] APR for patients with only perirectal lymph node metastasis

ISSN (O): 2687-5365; ISSN (P): 2753-6556

without iliac or inguinal lymph node metastasis seems to be curative.[20]

We also reviewed the results with multimodal therapy. Systemic cytotoxic chemotherapy with dacarbazine 250 mg/m2/day intra venous every 3 weeks is associated with a survival of 20% with a median response duration of only 4–6 months.[15] Temozolomide, the analogue of dacarbazine, at a dosage of 200 mg/m2/day orally for 5 days, every 4 weeks has the advantage of oral use and a lower rate of central nervous system relapse.[21] A four-drug combination known as Dartmouth regimen (dacarbazine, cisplatin, carmustine, and tamoxifen) does not have any survival benefit over single agent dacarbazine. Taxanes show marginal improved survival.[11,16]

Presence of c-KIT mutation in the tumour makes sorafenib or imatinib or dasatinib (particularly for CNS metastasis) a drug of choice.[22]

BRAF mutation is infrequent in anorectal melanomas and thus anti BRAF antibodies vemurafenib or trametinib or dabrafenib are of limited use.[23]

Immune-checkpoint inhibitors such as ipilimumab (antibody to cytotoxic T-lymphocyte-associated protein-4, CTLA4), nivolumab (anti-PD1 antibody), and pembrolizumab (anti-PD1 antibody) have been approved for the treatment of melanoma.[24-25]

Combined chemotherapy, anti-BRAF therapy, TKIs, and immune-checkpoint inhibitors remain important therapeutic options for these patients.

Limitations: Very small number of cases and limited follow up precludes generalisability.

CONCLUSION

Anorectal melanoma is a rare and aggressive malignancy and occasionally manifest as a part of neurocutaneous syndromes. Patients usually present with advanced disease and there is no standardized medical and/ or surgical therapy. Local resection, APR with or without pelvic and inguinal lymphadenectomy is performed depending on nodal involvement. However, the extent of lymphadenectomy does not affect overall survival. Adjuvant combined chemotherapy, TKIs, and immune-checkpoint inhibitors particularly in metastatic scenario remain important therapeutic options for these patients.

Conflict of interest: The authors have no conflicts of interest.

Funding: There was no involvement of any third party while conducting this study. No grants were taken from any institute or organization in the research process of this study.

Authors' contributions:

Rinki Das: Study design, concept, data collection and analysis, writing of manuscript and manuscript editing.

Ritankar Sengupta: Study design, concept, data analysis, manuscript editing.

Doyel Halder: Data collection, data analysis, manuscript editing.

Saurabh Das: Concept, manuscript editing.

Tanup Das: Data collection, data analysis, manuscript editing.

Sourav Chatterjee: Data collection

Jayanta Halder: Data Collection

Asim Kumar Manna: Concept, analysis, manuscript editing.

REFERENCES

1. Coté TR, Sobin LH. Primary melanomas of the esophagus and anorectum: epidemiologic comparison with melanoma of the skin. Melanoma Res. 2009 Feb;19(1):58-60. doi: 10.1097/CMR.0b013e32831ef262. PMID: 19430407.
2. Roy AC, Wattchow D, Astill D, Singh S, Pendlebury S, Gormly K et al. Uncommon Anal Neoplasms. Surgical Oncology Clinics, Volume 26, Issue 1, 143 – 161
3. D. M. Sinclair, G. Hannah, I. S. McLaughlin, R. S. Patrick, G. Slavin, A. M. Neville Malignant melanoma of the anal canal BJS November 1970, doi.org/10.1002/bjs.1800571103
4. Garutti M, Foffano L, Mazzeo R, Michelotti A, Da Ros L, Viel A et al. Hereditary Cancer Syndromes: A Comprehensive Review with a Visual Tool. Genes (Basel). 2023 Apr 30;14(5):1025. doi: 10.3390/genes14051025. PMID: 37239385; PMCID: PMC10218093.
5. Klas JV, Rothenberger DA, Wong WD, Madoff RD. Malignant tumors of the anal canal: the spectrum of disease, treatment, and outcomes. Cancer. 1999 Apr 15;85(8):1686-93. doi: 10.1002/(sici)1097-0142(19990415)85:8 < 1686::aid-cncr7>3.0.co;2-7. PMID: 10223561.
6. Stefanou A, Nalamati SP. Anorectal melanoma. Clin Colon Rectal Surg. 2011 Sep;24(3):171-6. doi: 10.1055/s-0031-1286001. PMID: 22942799; PMCID: PMC3311504. [presentation, of metastatic disease]
7. Malaguarnera G, Madeddu R, Catania VE, Bertino G, Morelli L, Perrotta RE et al. Anorectal mucosal melanoma. Oncotarget. 2018 Jan 2;9(9):8785-8800. doi: 10.18632/oncotarget.23835. PMID: 29492238; PMCID: PMC5823579.
8. Blessing K, Sanders DS, Grant JJ. Comparison of immunohistochemical staining of the novel antibody melan-A with S100 protein and HMB-45 in malignant melanoma and melanoma variants. Histopathology. 1998 Feb;32(2):139-46. doi: 10.1046/j.1365-2559.1998.00312.x. PMID: 9543670.
9. Morson BC, Volkstädt H. Malignant melanoma of the anal canal. Journal of Clinical Pathology 1963;16:126-132.
10. Heyn J, Placzek M, Ozimek A, Baumgaertner AK, Siebeck M, Volkenandt M. Malignant melanoma of the anal region. Clin Exp Dermatol. 2007 Sep;32(5):603-7. doi: 10.1111/j.1365-2230.2007.02353.x. Epub 2007 Mar 21. PMID: 17376215.
11. Paolino G, Didona D, Macrì G, et al. Anorectal Melanoma. In: Scott JF, Gerstenblith MR, editors. Noncutaneous Melanoma [Internet]. Brisbane (AU): Codon Publications; 2018 Mar. TABLE 2, Classifications of anorectal melanoma (AM) Available from: https://www.ncbi.nlm.nih.gov/books/NBK506984/table/chapter6.t2/ doi: 10.15586/codon.noncutaneousmelanoma.2018.ch6 [staging]
12. Brady MS, Kavolius JP, Quan SH. Anorectal melanoma. A 64-year experience at Memorial Sloan-Kettering Cancer Center. Dis Colon Rectum. 1995 Feb;38(2):146-51. doi: 10.1007/BF02052442. PMID: 7851168.
13. Droesch JT, Flum DR, Mann GN. Wide local excision or abdominoperineal resection as the initial treatment for anorectal melanoma? Am J Surg. 2005 Apr;189(4):446-9. doi: 10.1016/j.amjsurg.2005.01.022. PMID: 15820458.
14. Homsi, J., Garrett, C. Melanoma of the Anal Canal: A Case Series. Dis Colon Rectum 50, 1004–1010 (2007). https://doi.org/10.1007/s10350-007-0242-5

ISSN (O): 2687-5365; ISSN (P): 2753-6556

15. Row D, Weiser MR. Anorectal melanoma. Clin Colon Rectal Surg. 2009 May;22(2):120-6. doi: 10.1055/s-0029-1223844. PMID: 20436837; PMCID: PMC2780244.
16. Luke JJ, Schwartz GK. Chemotherapy in the management of advanced cutaneous malignant melanoma. Clin Dermatol. 2013 May-Jun;31(3):290-7. doi: 10.1016/j.clindermatol.2012.08.016. PMID: 23608448; PMCID: PMC3709980.
17. Yeh JJ, Shia J, Hwu WJ, Busam KJ, Paty PB, Guillem JG et al. The role of abdominoperineal resection as surgical therapy for anorectal melanoma. Ann Surg. 2006 Dec;244(6):1012-7. doi: 10.1097/01.sla.0000225114.56565.f9. PMID: 17122627; PMCID: PMC1856617.
18. Gervasoni JE Jr, Wanebo HJ. Cancers of the anal canal and anal margin. Cancer Invest. 2003 Jun;21(3):452-64. doi: 10.1081/cnv-120018238. PMID: 12901291.
19. Roumen R.M.H. Anorectal melanoma in The Netherlands: a report of 63 patients, European Journal of Surgical Oncology (EJSO),Volume 22, Issue 6,1996,Pages 598-601,ISSN 0748-7983, doi.org/10.1016/S0748-7983(96)92346-X.
20. Falch, C., Mueller, S., Kirschniak, A. et al. Anorectal malignant melanoma: curative abdominoperineal resection: patient selection with 18F-FDG-PET/CT. World J Surg Onc 14, 185 (2016). doi.org/10.1186/s12957-016-0938-x [APR local disease extent]
21. Paul MJ, Summers Y, Calvert AH, Rustin G, Brampton MH, Thatcher N, et al. Effect of temozolomide on central nervous system relapse in patients with advanced melanoma. Melanoma Res. 2002 Apr;12(2):175-8. doi: 10.1097/00008390-200204000-00011. PMID: 11930115.
22. Knowles J, Lynch AC, Warrier SK, Henderson M, Herlot AG. A case series of anal melanoma including the results of treatment with imatinib in selected patients. Colorectal Dis. 2016 Sep;18(9):877–82. PMID: 26546509
23. Pelosi E, Castelli G, Testa U. Braf-Mutant Melanomas: Biology and Therapy. Curr Oncol. 2024 Dec 3;31(12):7711-7737. doi: 10.3390/curroncol31120568. PMID: 39727691; PMCID: PMC11674697.
24. Vafaei S, Zekiy AO, Khanamir RA, Zaman BA, Ghayourvahdat A, Azimizonuzi H, et al. Combination therapy with immune checkpoint inhibitors (ICIs); a new frontier. Cancer Cell Int. 2022 Jan 3;22(1):2. doi: 10.1186/s12935-021-02407-8. PMID: 34980128; PMCID: PMC8725311.
25. D'Angelo SP, Larkin J, Sosman JA, Lebbé C, Brady B, Neyns B, et al. Efficacy and Safety of Nivolumab Alone or in Combination With Ipilimumab in Patients With Mucosal Melanoma: A Pooled Analysis. J Clin Oncol. 2017 Jan 10;35(2):226-235. doi: 10.1200/JCO.2016.67.9258. Epub 2016 Nov 7. PMID: 28056206; PMCID: PMC5559888.

ISSN (O): 2687-5365; ISSN (P): 2753-6556