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RESEARCH ARTICLE

PRIMARY ANORECTAL MELANOMA: CASE SERIES OF 3 CASES

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ABSTRACT

Anorectal melanoma is a very rare tumor of neuroectodermal origin with poor prognosis because of delay in diagnosis. It is often mistaken for benign conditions such as hemorrhoids or rectal polyps. Surgical treatment ranges from local excision to radical abdominoperineal resection. Because of its rarity only few cases have been published in literature. Herein, we report series 3 case of anorectal malignant melanoma and further review management in light of the relevant literature.

INTRODUCTION

Anorectal melanoma is a rare tumor of neuroectodermal origin, with < 700 cases reported since first being reported by Moore in 1857 (Moore, 1857). Anorectal melanomas (AMs) compose fewer than 1% of all malignant melanomas and fewer than 3% of all anal tumors (Chang *et al.*, 1998). They are usually diagnosed between the sixth and eighth decades of life and have a female predilection (Van Schaik *et al.*, 2008). Symptoms are nonspecific, and as a result patients tend to have large lesions and/or advanced disease at presentation. Patients usually present with rectal bleeding or altered bowel habits (Singer and Mutch, 2006). It is often mistaken for benign conditions such as hemorrhoids or rectal polyps. The absence of early clinical manifestations and lack of clinical suspicion contribute for delayed diagnosis (Van Schaik *et al.*, 2008). Up to 60% of the cases have metastasis at the time of diagnosis (Gavriilidis *et al.*, 2013). Therefore, disease recurrence and disease-related morbidity and mortality are high, with 5-year survival rates ranging from 0% to 30% (Buissin *et al.*, 2015). Treatment is primarily surgical which ranges from local excision to radical abdominoperineal resection. Because of its rarity case series of only few cases have been published in literature. We present here a case series of 3 cases over a period of 10 months.

MATERIALS AND METHODS

The study was carried out in the department of pathology at Sheri-i-Kashmir Institute of Medical Sciences, Kashmir India. A total of 3 cases collected over a period of 10 months from 1st January 2018 to 1st October 2018 who underwent surgery for anorectal mass and diagnosed as Primary anorectal melanoma were included in the study. The age, sex, relevant clinical and radiological details were recorded for each case. The specimen was processed as per standard procedure. 4-5mm thick sections were cut on microtome and stained by hematoxylin and eosin stain. The stained slides were studied in detail microscopically; and Immunohistochemistry was done for confirmation.

Case presentation

55 year old male presented with chief complaints of bleeding per rectum from 1 year and something coming out from anus from 6 months. On examination patient was conscious oriented. P/A no mass was palpable. A Rt inguinal region swelling measuring 3x3 cms in size. Firm in consistency was however palpated. Swelling tethered to underlying structures. On DRE firm Non tender swelling was palpable externally b/w 9-12 o'clock internally extending between 9-3 o'clock. Deep margin could not be appreciated. Mucosa over swelling fixed. CECT SHOWED large heterogeneously enhancing mass lesion mainly in left lateral wall seen in anorectal region. Stranding was seen in pararectal fat. Regional lymph nodes were enlarged with grade II prostatomegaly and cystitis. E/L with APR with groin dissection with Sartorius hip over cover

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was done. Approximately 10x5 cms of rectal thickening extending from AV upto 5cms upwards. Mass was compressing 30-40% of circumference RWQ. On Gross examination Abdominoperineal resection specimen was received with right groin dissection. TME was partially complete. Specimen measured 30x5 cms in size. On cutting open a large ulceroinfiltrative pigmented growth identified in anal canal measuring about 10x 5cms about 5 cms from anal end. Growth was infiltrating into perirectal fat. M/E showed tumor comprising of pleomorphic tumor cells arranged in sheets as well scattered having individually enlarged nuclei, prominent eosinophilic nucleoli and moderate amount of cytoplasm. Melanin pigment was seen within the tumor cells as well as extracellularly. Tumor was mitotically very active. Depth of invasion was 4mm. Features were those of Ano rectal malignant melanoma. Multiple tumor nodules identified in mesorectum. 7 lymph nodes identified of which 3 showed metastatic deposits of same tumor. AJCC staging; Stage III.

Case 2. 50 old female presented with constipation from 7 months and history of bleeding per rectum from 5 months. She was a known case of hypertension. By digital rectal examination, there was a mass about at anal verge. Rectosigmoidoscopy showed an ulceroproliferative growth extending upto 5cm from anal verge. Biopsy showed submucosal infiltration by tumor cells having eosinophilic cytoplasm prominent nucleoli. and coarse melanin pigment seen. Diagnosis of anorectal melanoma was made. Computed Tomography (CT) showed circumferential thickening involving rectum. Large perilesional nodes also seen. Abdominoperineal resection was done. HPE showed features of anorectal melanoma.

Case 3, 56F presented with 7 months history of bleeding per rectum and something coming out. On DRE Polypoidal mass was felt at anal verge. Rectosigmoidoscopy showed a polypoidal lesion about 1 cms from anal verge. CT showed Heterogeneously enhancing intraluminal polypoidal lesion of approx. size 5x4x3 cm, APR was done. On gross examination polypoidal lesion measuring about 5x5 cms was seen at anal verge. Growth was grey/brown with grey /white areas. Histopathology showed features suggestive of anorectal melanoma.



Figure 2. Gross picture showing specimen of APR with large ulceroproliferative pigmented growth measuring 12x 7cms at anal verge and extending about 5cms upwards.(10x)



Figure 3. Gross picture showing a polypoidal growth about 3x3 cms at anal verge.(10x)



Figure 1. CT SCAN abdomen showing large heterogeneously enhancing mass lesion mainly in left lateral wall seen in anorectal region. Stranding seen in pararectal fat

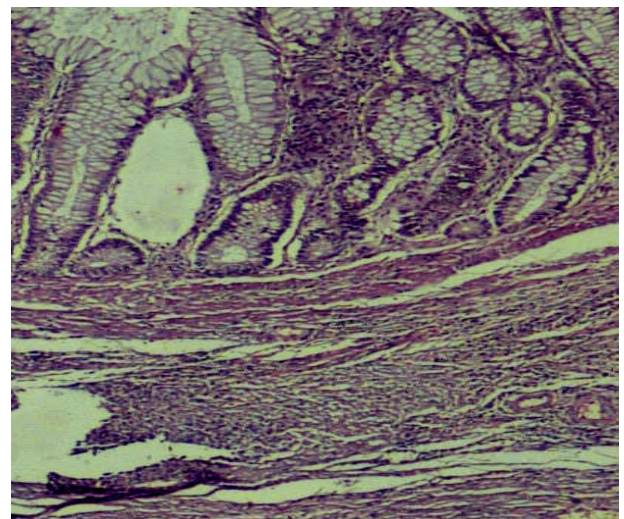


Figure 4. Photomicrograph of malignant melanoma showing submucosal infiltration by tumor cells(10x)

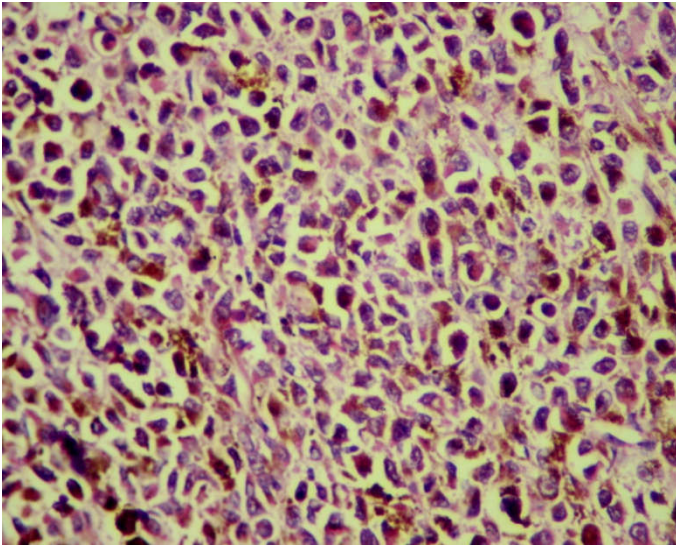


Figure 5. Photomicrograph of malignant melanoma showing dense pigment within melanoma cells and outside.(10x)

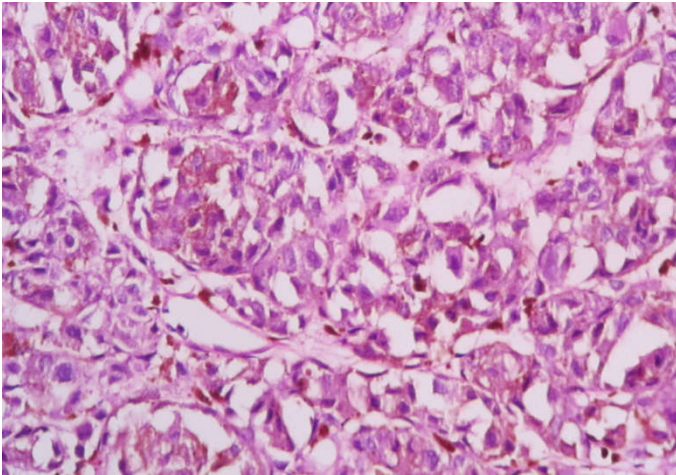


Figure 6. Photomicrograph of malignant melanoma showing tumor cells having prominent nucleoli, abundant cytoplasm and coarse brown pigment.

DISCUSSION

Anorectal melanoma is a rare condition accounting for 0.2%-3% of all melanoma cases and 0.1%-4.6 % of all malignant tumors of the rectum and anus (Chang *et al.*, 1998; Van Schaik *et al.*, 2008). The incidence of ano-rectal melanomas has significantly increased over the last two decades which may be attributed either to actual rise in the number of cases or improved diagnostic techniques (Khan *et al.*, 2014). Anal melanoma normally originates in the transition zone above the dentate line, where melanocytes normally occur. Melanoma is defined as "rectal" when it occurs in the rectum above the anorectal junction, whereas the anal canal is below anorectal line. The anorectum is the third most common site for melanoma after the skin and eyes and the most frequent location of primary gastrointestinal tract melanoma (Chang *et al.*, 1998). Usually it affects women in the fifth or sixth decade and patient presents with rectal bleeding or altered bowel habits (Van Schaik *et al.*, 2008; Gavriilidis *et al.*, 2013). The absence of early clinical manifestations and lack of clinical suspicion contribute for delayed diagnosis. Up to 60% of the cases have metastasis at the time of diagnosis (Buissin *et al.*, 2015). The abundant lymphatics of the anorectum probably provide a pathway for the high rate of inguinal and iliac lymph

node metastases (Correia *et al.*, 2008). The rich vascular network in this area promotes hematogenous spread to liver, lung, bone, brain, and other organs. Radiological investigations should be directed at these organs. The mean survival time has been reported to range from 18 months to 23 months (Alberto Julius Alves Wainstein *et al.*, 2011). Grossly, the majority of lesions appears polypoid, with or without pigmentation, and can be ulcerated as well (Chute *et al.*, 2006). The tumor is amelanotic in about 30% of the cases, and with considerable morphologic variability, misdiagnosis as lymphoma, carcinoma or sarcoma is common (Sahoo *et al.*, 2013). The use of immunohistochemistry panels, including S-100 proteins, Melan A, HMB-45 and tyrosinase, can help in the diagnosis (Chute *et al.*, 2006). The factors for poor prognosis includes, advanced disease at the time of the diagnosis and rich vascularity which increases the risk of hematogenous metastasis. The staging of anal melanoma differs from that of cutaneous melanoma, which is based primarily on thickness in millimeters (Breslow classification). Anal melanoma is staged on a clinical basis, focusing on locoregional and distant spread. Stage I is local disease only, stage II is a local disease with regional lymph nodes, and stage III is distant metastatic disease (Singer and Mutch, 2006). Using the TNM classification, melanomas are grouped into 4 numbered stages. Staging is defined as follows: (1) stage I, no positive lymph nodes and no sign of cancer spread; melanoma is < 2 mm thick or < 1 mm thick and ulcerated; (2) stage II, no positive lymph nodes and no sign of cancer spread; melanoma is > 2 mm thick or > 1 mm thick and ulcerated; (3) stage III, positive lymph nodes and no sign of cancer spread; (4) stage IV, melanoma has spread elsewhere in the body, away from the primary site (Chang *et al.*, 1998). Treatment of anorectal melanoma is primarily surgical (Bullard *et al.*, 2003). Abdominoperineal resection (APR) with or without inguinal lymph node dissection or wide local excision (WLE) are the treatment options available (Brady *et al.*, 1995; Bullard *et al.*, 2003). Abdominal perineal resection has historically been the initial surgical treatment of choice for anorectal melanoma and is still advocated by some institutions.

The difference in Five-year survival rate between patients undergoing APR versus WLE (17% & 19%, respectively) is not significant (Iddings *et al.*, 2010). As overall prognosis of anorectal melanoma is poor, the surgical approach is to be individualized, the choice of ideal surgical procedure is still debatable with some recent studies emphasizing that sphincter saving local excision with loco-regional radiotherapy is apt for small tumours and it results in lesser morbidity. While for larger and obstructing tumors abdomino-perineal resection (APR) should ideally be done. The role of adjuvant chemotherapy is controversial however, malignant melanoma owes its aggressiveness to loss of c-kit and hence, tyrosine kinase inhibitors like imatinib may prove beneficial (Khan *et al.*, 2014). Immune mediators like interferon 2 alpha and interleukin 2 may also play some role in patients with metastatic malignant melanoma (Praveen *et al.*, 2014). Adjuvant radiation therapy is well tolerated and is promising in improving locoregional control. Postoperative radiotherapy may improve locoregional control after wide local excision. Definitive assessment of the efficacy of adjuvant radiation therapy requires further prospective studies. No published randomized trials are available for anal melanoma due to the small number of patients requiring several decades to recruit in most series. Hence, all treatment regimens are extrapolated from trials involving metastatic cutaneous melanoma (Praveen

et al., 2014). Despite of all these treatment modalities prognosis is still grave for the patient and depends on the depth of invasion, stage, duration, size of the tumor and lymph node status.(2,9.The 5 year survival rates for patients with local, regional and metastatic ano-rectal malignant melanoma are 32%,17% and 0% respectively (Lanka Praveen et al., 2014). The rarity of this disease and the limited number of patients who present with stage I disease have prevented definitive trials examining the optimal treatment of curable anal melanoma. In addition, much information has been derived or extrapolated from the cutaneous melanoma literature, which is not always a valid comparison. A well-conducted, adequately powered randomized trial may never occur because of the relative infrequency of this entity. The decision remains unclear.

Conclusion

Anorectal melanoma although a rare entity should be kept in the differential diagnosis for lesions arising in the anorectum. As there is no consensus regarding management of Anorectal melanoma, management should therefore be individualized.

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