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Anal melanomas: The sun does not shine on this mucosa

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Cutaneous melanomas are rare in the Indian population and mucosal and anorectal lesions are seen but very occasionally. They often masquerade as hemorrhoids leading to delay in diagnosis. This was a retrospective study done in Sri Ramachandra University, where hospital records were perused to record all cases of anal melanomas. Abdomino-perineal resection and wide local excision offer equal survival rates. Novel targeted therapy represents the cutting edge of therapy today.

Key words: Anorectal, malignant melanoma, surgical treatment.

INTRODUCTION

Anal melanomas are uncommon malignancies which account for less than 1% of all melanomas. The anal region is the third most common location for malignant melanomas after the skin and the eye. There are very few meta analyses available given the small number of patients seen. The presence of receptors on melanoma cells is promising as it paves the way for targeted therapy. This study presents small series and review treatment options available for this tumor.

The aim of this study was to look at the presentation of anal melanomas at our institution, analyse the treatment options and review literature.

PATIENTS AND METHODS

This was a retrospective study done in Sri Ramachandra Medical College and Hospital, Sri Ramachandra University, Chennai, India between January 2005 and 2011. Case records, operative registers and histopathology files were perused, data were collected and analyzed.

Demographics

A total of 21 patients constituted the melanoma study population of over a 6 year period. There were 12 male and 9 female patients. There were 10 patients with anal melanomas (8 male and 2 female patients). There was maximum clustering in the 8th decade of life closely followed by the 6th decade (Figure 1).

The patients with anal melanomas present with complaints of bleeding per rectum and were initially thought to be hemorrhoids on primary survey. Digital and proctoscopic examination showed polypoidal or ulcerated lesions on palpation and there was surrounding induration. The lesions were found at the anal verge and up to 3 cm proximally (Figure 2). Six patients had associated pruritus and 2 patients had inguinal lymphadenopathy at presentation. One patient also complained of mucoid blood tinged discharge. Sixty four percent of the patients present with alteration in defaection, not amounting to constipation.

The patients had a visible black brownish lesion on proctoscopic examination, which on punch biopsy was confirmative for malignant melanoma. Computerized tomography showed the lesion with surrounding edema. Metastatic workup showed extension to the liver, lungs and brain in 2 patients. Histology showed anal glands with clusters of malignant cells with pleomorphic nuclei and

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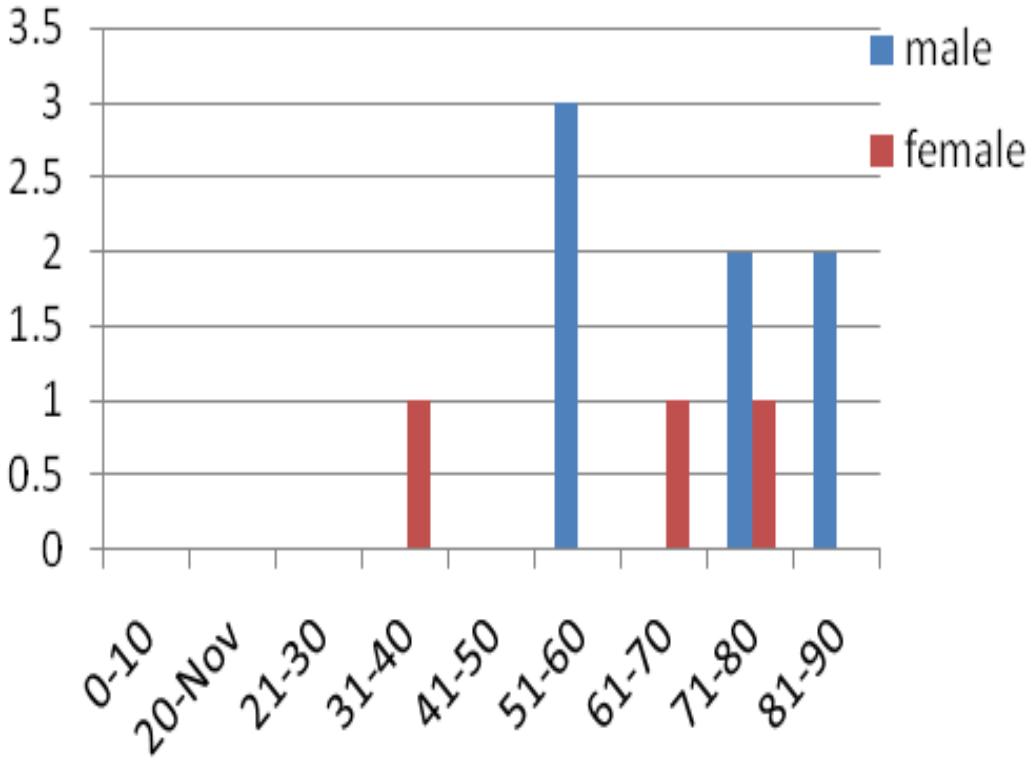

Figure 1. Age and gender demographics.

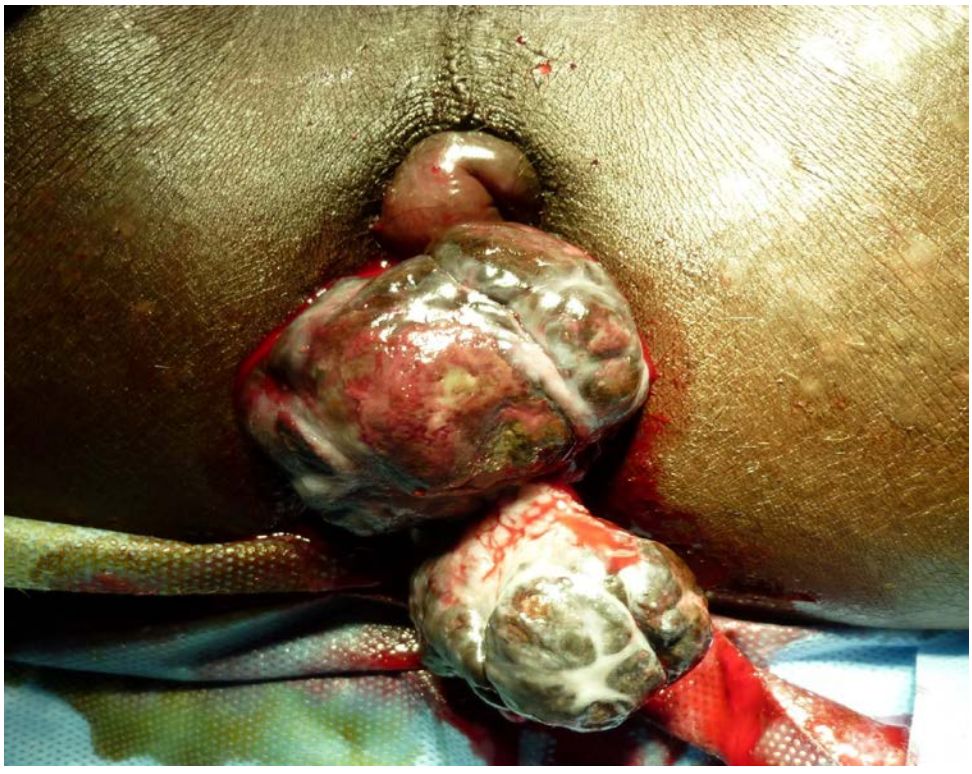

Figure 2. The anal melanoma prolapsing through the anal verge.

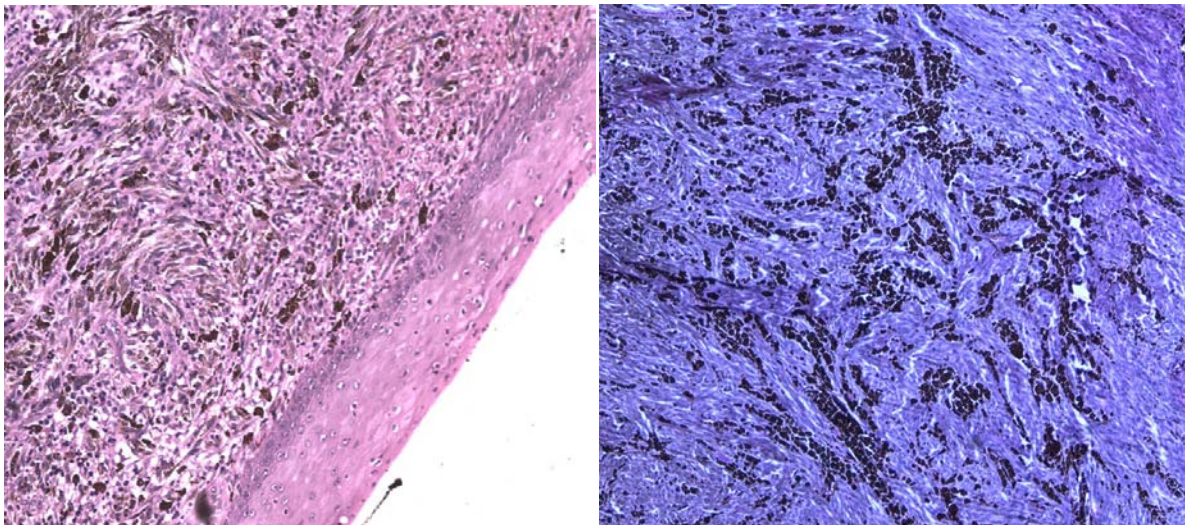

Figure 3. Anal glands with clusters of malignant cells with melanin pigment.

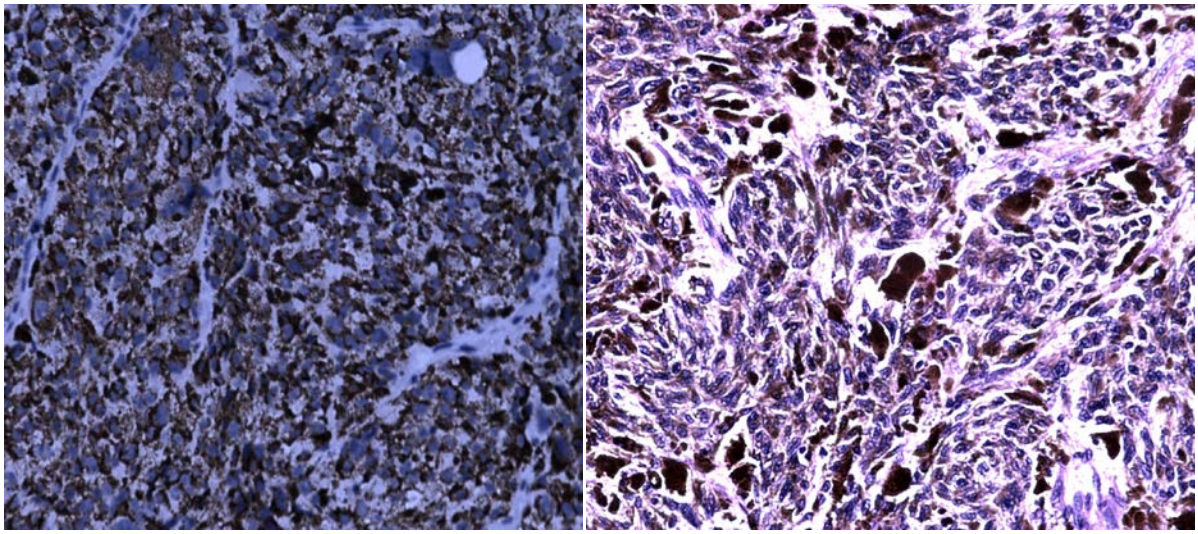

Figure 3. The IHC positivity for HMB 45.

abundant melanin pigment (Figure 3). The immunohistochemistry when done was positive for HMB 45, the melanosome protein (Figure 4).

Treatment

The 2 patients with metastases were referred for palliative chemotherapy. Of the remaining 8 patients with anal melanoma, 6 patients underwent abdomino perineal resection (APR) and four patients underwent wide local excision (WLE). All patients received post operative chemotherapy with cisplatin, vinblastine and dacarbazine. The patients who received palliative chemotherapy for metastatic disease died within two months. Of the 8 patients who underwent operative treatment, 3 were lost to follow up. Of the remaining 5 patients, 4 were dead at twelve months (3 of the APR group and 1 who underwent WLE). The lone patient survived for fourteen months and had undergone APR.

RESULTS AND DISCUSSION

Anal melanomas were described by Moore (1857) and account for 3 to 5% of all large bowel malignancies. The incidence is less than 1% and is higher in males, in black men and increases with age. Squamous cell carcinoma is the most common anal malignancy and is followed by cloacogenic malignancies. Melanomas in the anal canal

arise from the melanocytes which occur in the squamous mucosa distal to the dentate line. The lesions can be in the rectum, anal canal or both with majority arising from the dentate line. They tend to spread sub mucosally and by the time they cause symptoms, they are often beyond surgical cure. Rectal melanomas account for less than 3% of all melanomas and are more common in females as compared to males (McLaughlin et al., 2005; Wanebo et al., 1981; Ramakrishnan et al., 2008). Once a rectal mass is noted, pigmentation is a clue for diagnosis of melanoma; however, macroscopic pigmentation is not always present.

The patients present with bleeding, diarrhea, tenesmus and severe pain on defaecation (Wanebo et al., 1981; Ramakrishnan et al., 2008). The black brown ulcero-proliferative tumor is often visible and is always palpable as a nodule or induration, without or with inguinal lymphadenopathy (20%). The differential diagnosis includes thrombosed pile mass, prolapsing polyp or rectal carcinoma. The porto-systemic anastomosis of this area makes it possible for metastases (38%) to the liver, lung, brain, bone and other organs. Digital examination provides information about size, fixation, and ulceration of the lesion. Endoluminal ultrasound evaluates the tumor thickness and nodal status. Biopsy is confirmative in all patients and amelanotic melanomas also occur. Singluff classification grades anorectal melanomas as stage 1 (localized tumor), stage 2 (regional node metastasis) and stage 3 (distant metastasis).

There are often occult metastases at diagnosis and patients continue to die as late as 11 years after diagnosis and therapy. The survival depends on the staging and is not dependent on the surgical radicality. Historically, there was great enthusiasm for APR along with bilateral prophylactic groin dissection and sometimes even pelvic exenteration. However, long survivals were noted even after wide local excision and no difference in survival was noted when the tumors were compared by similar stages. Thibault et al. (1997) showed a survival rate of 22% at five years with APR while WLE showed a five year survival of 16%. Other series have showed no survival benefit between APR 19% and WLE 18%. WLE has less morbidity than APR and avoids a colostomy. Bullard et al. (2003) showed that in a series of 15 patients, there was no difference in local recurrence, systemic recurrence, disease free survival or overall survival between the APR group and the WLE group. Zhang et al. (2010) showed a higher local recurrence with APR versus WLE even though there was no survival advantage. It is important to give three dimensional clear margins in WLE which is possible in small tumors and lesions which are polypoidal. Large tumors are better managed with an APR even though it necessitates a colostomy. The presence of perineural invasion is an important prognostic factor (Ueno et al., 2001). Ballo et al. (2002) demonstrated that adjuvant radiation controls loco regional disease after WLE.

Adjuvant and neoadjuvant radiotherapy also improves loco regional control, even though it was not offered in any of our patients. Chemotherapy with interferon, interleukin 2, cisplatin, vinblastine, and dacarbazine is effective in the adjuvant setting (Brady et al., 1995). However, no randomized controlled trial data is available given the rarity of these lesions. There is a report of disappearance of liver metastases in a patient with combination dacarbazine, adriamycin and vincristine (Sasaki et al., 2010).

Genetic alterations are found within the receptor tyrosine kinase signaling pathways in cutaneous melanomas, and include *BRAF* point mutation, *NRAS* point mutation, *KIT* point mutations, *EGFR* amplification, *PTEN* gene deletion, *AKT* point mutation and EGFR 2 mutations (Curtin et al., 2005). BRAF mutations documented in 59% of cutaneous melanomas are seen in 3% of mucosal melanomas. Sorafenib is a bis-aryl urea with potent activity against *BRAF*. Sorafenib inhibits VGEF, PDGFR β and KIT. Targeted therapy promises to be the way ahead.

Conclusion

Anorectal melanomas represent both a diagnostic and therapeutic challenge because of its nonspecific presentation and rarity. Immunocytochemical studies that aid diagnosis includes S 100, HMB 45, micropthalmia associated transcription factor (Mitf), tyrosinase, and Melan A (MART 1). Five years survival is as low as 20% in anorectal melanomas, the possible reasons being delay in diagnosis, inherent aggressiveness of tumor biology and early dissemination of the disease as a result of close contact with the rich lymphovascular supply of the underlying anorectal mucosa.

REFERENCES

Ballo MT, Gershenwald JE, Zagars GK, Lee JE, Mansfield PF, Strom EA, Bedikian AY, Kim KB, Papadopoulos NE, Prieto VG, Ross MI (2002). Sphincter-sparing local excision and adjuvant radiation for anal-rectal melanoma. J. Clin Oncol. 20(23):4555-4558.

Brady MS, Kaxolius JP, Quan SH (1995). Anorectal melanoma. A 64-year experience at Memorial Sloan-Kettering Cancer Center. Dis. Colon Rectum 38(2):146-151.

Bullard KM, Tuttle TM, Rothenberger DA, Madoff RD, Baxter NN, Finne CO, Spencer MP (2003). Surgical therapy for anorectal melanoma. J. Am. Coll. Surg. 196(2):206-211.

Curtin JA, Fridlyand J, Kageshita T, Patel HN, Busam KJ, Kutzner H, Cho KH, Aiba S, Bröcker EB, LeBoit PE, Pinkel D, Bastian BC (2005). Distinct sets of genetic alterations in melanoma. N. Engl. J. Med. 353(20):2135-2147.

McLaughlin CC, Wu XC, Jemal A, Martin HJ, Roche LM, Chen VW (2005). Incidence of non cutaneous melanomas in the US. Cancer 103(5):1000-1007.

Ramakrishnan AS, Mahajan V, Kannan R (2008). Optimizing local control in anorectal melanoma. Indian J. Cancer 45(1):13-19.

Sasaki S, Kojima T, Hidemura A, Hatanaka K, Uekusa T, Ishimaru M (2010). A case report of anorectal malignant melanoma showing a complete response after DTIC/ACNU/VCR therapy. Gan To Kagaku Ryoho 37(10):1999-2002.

Thibault C, Sagar P, Nivatvongs S, Ilstrup DM, Wolff BG (1997). Anorectal melanoma-an incurable disease. Dis. Colon Rectum 40(6):661-668.

Ueno H, Hase K, Mochizuki H (2001). Criteria for extramural perineural invasion as a prognostic factor in rectal cancer. Br. J. Surg. 88(7):994-1000.

Wanebo H, Woodruff JM, Farr GH, Quan SH (1981). Anorectal melanoma. Cancer 47(7):1891-1900.

Zhang S, Gao F, Wan D (2010). Abdomino perineal resection or local excision? A survival analysis of anorectal melanoma with surgical management. Melanoma Res. 20(4):338-341.