International Journal of Medical Research Professionals

*Case Report*

# Malignant Melanoma –An Exceptional Survival of Five Years

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**Article History**
Received: 10 Oct2015
Accepted: 15 Oct2015

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**ABSTRACT**

Anorectal melanoma is an uncommon cancer of the anal canal. It is usually misdiagnosed with common benign conditions like haemorrhoids, anal fissure, anal polyp etc. Most patients have distant metastasis at the time of diagnosis. Surgery if feasible is the preffered treatment for both primary and metastatic melanomas. There is no proven role of adjuvant and systemic therapy for metastatic anal melanoma. It is associated with a poor prognosis and overall survival.We report here a case of metastatic anorectal melanoma surviving for more than five years.

**KEYWORDS**: Adjuvant chemotherapy radiotherapy, Inguinal lymph node, Metastatic anorectal melanoma.

## INTRODUCTION

Melanoma is a neoplasm of the melanocytes which are embryologically derived from the neural crest cells . Anal melanoma is thought to arise from normal melanocytes distal to the dentate line that extend proximally into the rectum[1]. Anal canal is the most common site of GI mucosal melanoma and accounts for less than 1% of all anal malignancies[2]. The incidence rate is reported as 0.4% per million[3]. 0.4%–3.0% of all malignant melanoma are anorectal melanoma[4]. The reported 5-year overall survival rate is 6%–15% after surgery[4]. Casucian females in their sixth-eighth decade are commonly affected[5]. Misdiagnosis as benign conditions early infiltration and distant spread result in poor overall survival. Unlike cutaneous melanoma there are no associated risk factors[6]. Most preferred treatment is surgery if it is feasible. Adjuvant radiotherapy and chemotherapy are used to improve survival[7]. The 5 year survival rate is less than 20%[8]**.** We present here a case of mucosal melanoma with metastasis to liver surviving for 5 years after receiving adjuvant chemotherapy and radiotherapy.

## CASE REPORT

A 65 years old male presented with passage of urine We report here a case of a 42 year old lady who presented to our hospital GMCH Nagpur in November 2010 with complaints of swelling in right inguinal region associated with pain since 4 months. On examination the swelling was 3×2cm with firm to hard consistency. She also gave history of excision of rectal polyp, hemorrhoids in 2009 whose histopathology report was suggestive of spindle cell morphology poorly differentiated carcinoma - Melanoma. She went to TMH hospital for further investigations where IHC was performed and the tumour cells were found to be positive for S100 and negative for HMB45 Melan A EMA CD34, Desmin favoring melanoma over malignant peripheral nerve sheath tumour. FNAC from the node was positive for deposits of malignant melanoma. She received six cycles of decarbazine vinblastin and cisplatin based chemotherapy from November 2011 to April 2011. After 6 cycles of chemotherapy clinically no inguinal lymph nodes were palpable. Her post 6 cycles chemo CT Abdomen revealed subcentrimetric pelvic lymphadenopathy. She recieved local radiotherapy to pelvic region 40 GY 20 fractions from August 2011 to Sept 2011. Clinical and Radiological examination was normal. She was disease free from 2011-April 2015. In April 2015 she came to OPD with complaints of pain in abdomen. Her contrast enhanced CT scan of abdomen revealed liver metastasis throughout liver parenchyma largest of 7mm×7mm with perirectal and perianal fat stranding and on local examination there was no growth. Decarbazine and Cisplatin based chemotherapy was commenced from May 2015 as she was not affording higher molecule treatment.

## DISCUSSION

Melanoma is a radio and chemo resistant disease and no systemic therapy is considered standard. Malignant melanoma of anorectal region is the third most common melanoma after skin and ocular**.**

The most common symptoms are pain and bleeding from per anum, tenesmus, and changes in bowel habits. Common investigations performed are Digital Rectal Examination Proctoscopy Colonoscopy, Biopsy and Contrast Enhanced CT scan of Abdomen to know the extent of the disease. Endoluminal ultrasound is used to determine the tumor thickness nodal status and also helps in delineating lesions amenable to WLE. FNAC from the inguinal lymph nodes is performed to

determine the presence of lymph nodal metastasis. Immunohistochemical stains for Melanoma antigens S- 100, HMB - 45, and vimentin can also be performed[9]. Epidermoid carcinoma is differentiated from melanoma by polyclonal antiserum carcinoembryonic antigen (CEA) and monoclonal antibodies to CEA[10].

**Fig1: Rectal polypectomy scar in our patient**

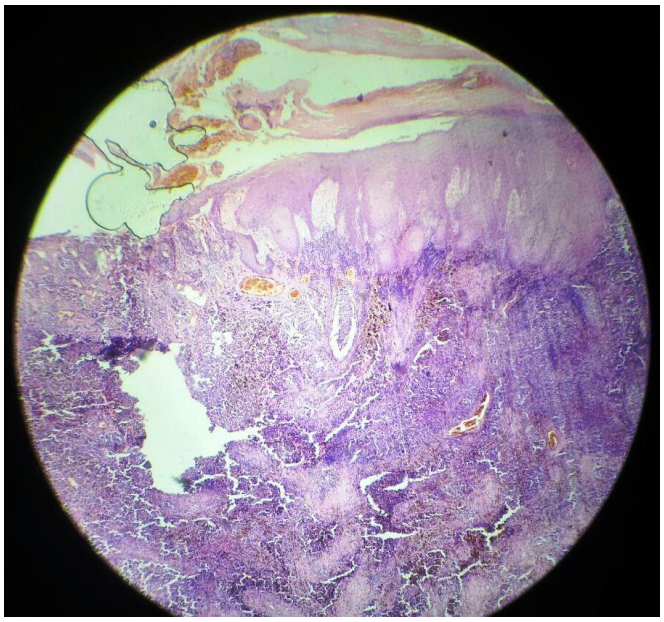

**Fig2: 10X section shows stratified squamous epithelial lining. Underlying tissue shows tumour arranged in sheets**.

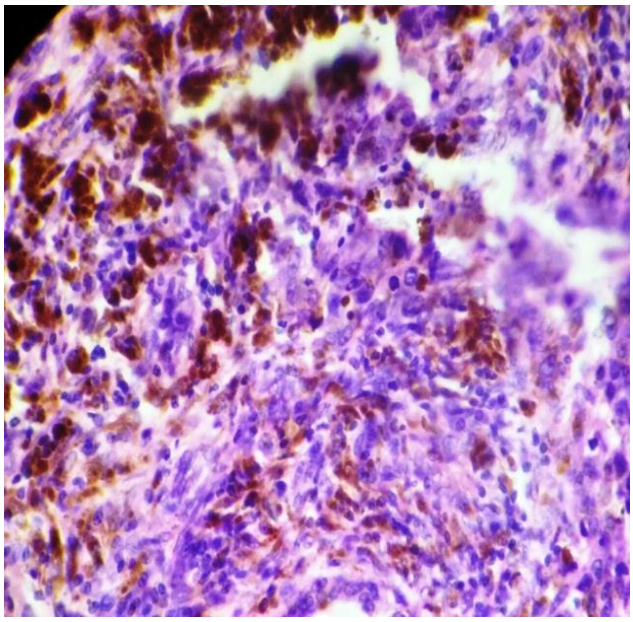

**Fig3: 100 Xsection shows the presence of intracytoplasmic brown coloured pigment suggestive of melanoma.**

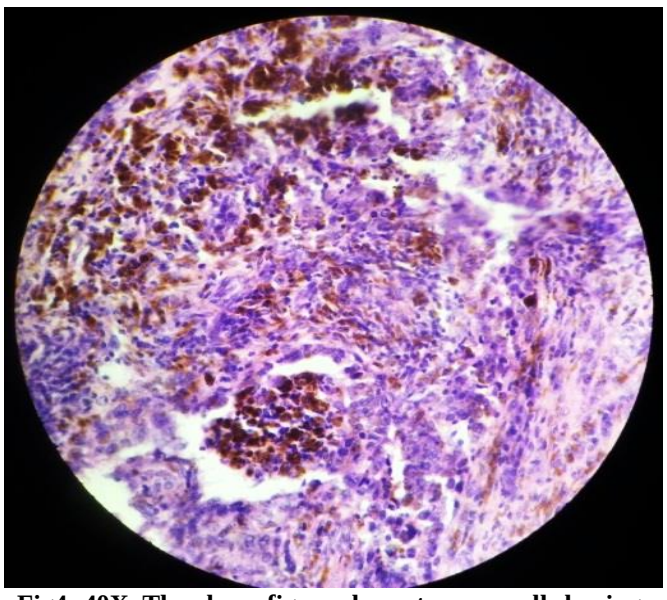

**Fig4: 40X, The above figure shows tumour cells having indistinct moderate amount of cytoplasm, oval nuclei with prominent nucleoli with irregular margin.**

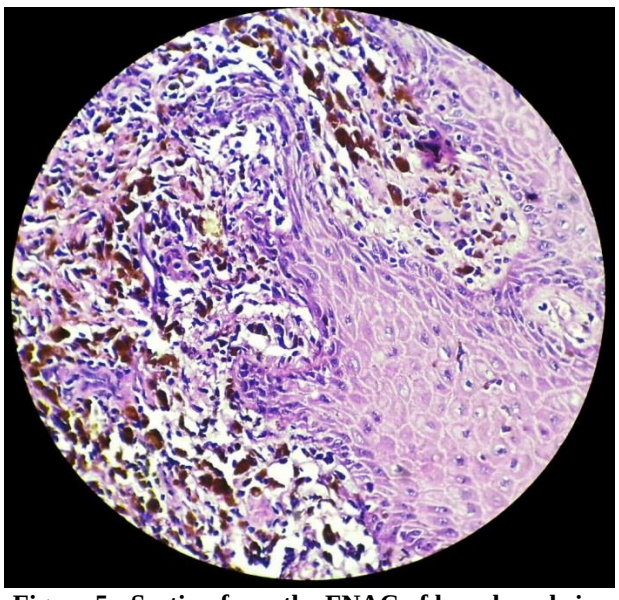

**Figure 5: Section from the FNAC of lymph node in 40 x magnification showing tumour cells harboring melanin pigment intracytoplasmically**.

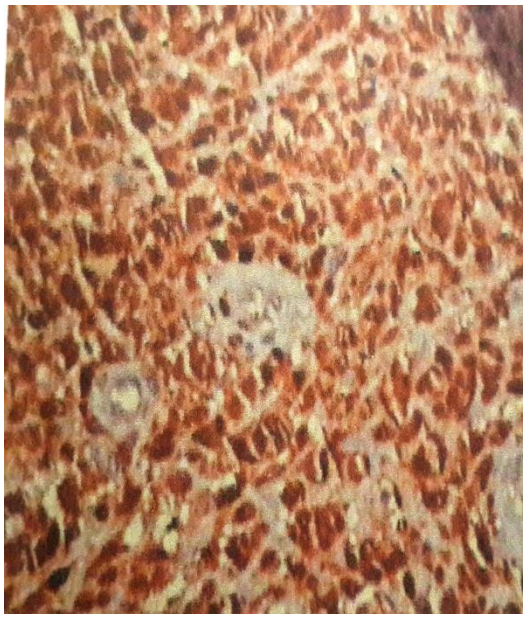

**Figure 6: Showing S-100 positivity on Immunohistochemical evaluation.**

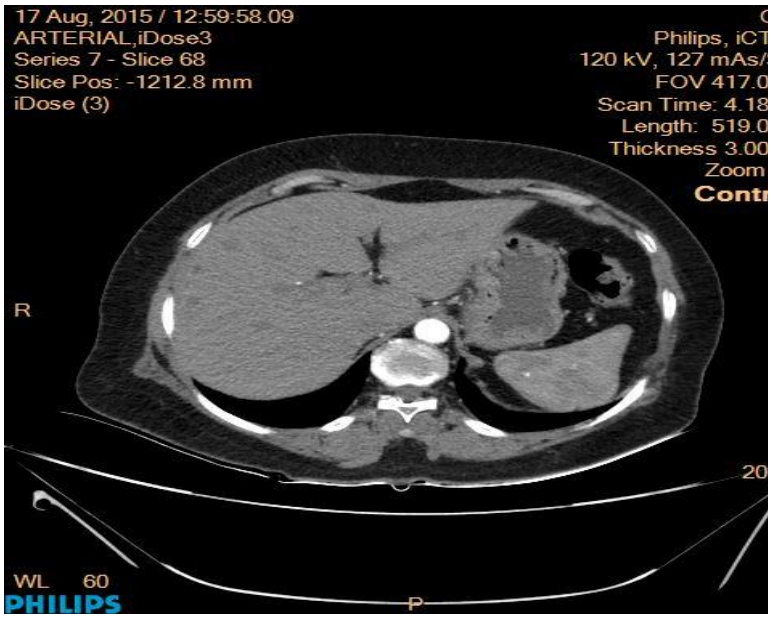


**Figure 7: Contrast enhanced CT scan shows multiple liver metastasis spread throughout the liver parenchyma.**

Our subject had presented with past history of pain during defecation and swelling in the inguinal region. She had undergone excision for rectal polyp causing pain per anum. She was evaluated by IHC repeated contrast enhanced CT scan of abdomen regularly at 6monthly intervals. Our subject was incidentally diagnosed with liver metastasis in one of the latest scan as seen in Fig 7.

Surgical excision in the form of APR, WLE and TAE trans anal excision is the definitive treatment. TAE[11] is preferred as it reduces morbidity and chances of local recurrences. It is also recommended to perform sentinel lymph node biopsy alongside TAE[11]. Yeh et Al. reported that there was no significant difference in the local recurrence after APR or TAE[11]. Pessaux et al. recommended APR for large tumours and isolated local recurrences[12]. Wide local excision is undertaken when negative margins can be achieved. WLE favours early recovery and no colostomy in comparison to APR. Thibault and colleagues reviewed 50 cases and observed no difference in survival in patients treated by WLE or APR[13]. Lymph node dissection is preferred for clinically palpable lymph node dissection[14]. Our patient underwent local excision in the form of polypectomy. Figure 1 shows rectal polypectomy scar in our patient. Figure 2, 3 and 4 show the microscopic findings of tumour cells with oval hyperchromatic and pleomorphic nuclei and intracytoplasmic melanin pigment in tumour cells. Figure 5 show the presence of intracytoplasmic melanin pigment in the specimen of inguinal node FNAC and S-100 positivity is seen in figure 6 on Immunohistochemical evaluation.

Decarbazine was earlier used as a single agent and had median response duration of 4-6 months. Combination chemotherapy known as the Dartmouth regimen: Dacarbazine, Cisplatin Carmustine, and Tamoxifen have shown an improved response rate (19%) over dacarbazine alone. (10%)[15]. Side effects like bone marrow suppression, nausea and vomiting are more pronounced with combination chemotherapy[16].

Biochemotherapy a combination of interferon (IFN), inter leukin-2 and cytotoxic drugs which include cisplatin, vinblastin and decarbazine has been developed. Kim and colleagues at M.D.Anderson observed a median survival of 12 months with biochemotherapy as compared to chemotherapy alone[17]. BRAF and KIT proto oncogene mutation are commonly associated with both cutaneous and anal melanoma. Vermufenib[18] BRAF inhibitor and Ipilimumab[19] a monoclonal antibody against CTLA-4 has shown a limited role in metastatic mucosal melanoma. In our case Vinblastin, Cisplatin and Decarbazine combination chemotherapy was administered excellent response was observed and she has been resumed on the same protocol after diagnosis of liver metastasis due to financial constraints.

Role of radiotherapy is limited to post-operative and palliative settings[20]. Bujko and colleagues reported better local control. In preoperative settings no significant benefit has been observed[21]. A study conducted by Ballo et al. in M.D Anderson where radiotherapy was delivered in post-operative settings in a hypo-fractionated regimen of 30 Gy (5 fractions over 2.5 weeks). The 5-year local control rate was found to be 74%, with a 5-year disease-specific survival of only 36%[22]. Palliative radiotherapy in case of recurrent metastatic and unresectable disease is effective. No difference in survival is found after surgical and radiotherapeutic management[22]. IMRT reduces radiotherapy side effects like skin toxicity, interruptions during treatment, and better local control[23]. Gupta and colleagues recommended that local recurrence after resection can be prevented by interstitial brachytherapy

with cesium137[24]. Lymphedema and procitis are common toxicities when inguinal /pelvic nodes are included in the radiation fields[25]. Radiotherapy to inguinal nodes was planned with a radical and curative intent in our case 100% response rate with survival of more than 5 years was been observed.

Snoj et al. devised electrochemotherpay in an inoperable patient where he increased the permeability of the tissues to chemotherapeutic agent – cisplatin by giving electrical pulses and found significant reduction in the size of the primary after 5 appplications with a total dose of 6mg of cisplatin. The patient was then subjected to surgery which was followed by intracavitatory radiotherapy by Cesium 137 for the primary. However the patient developed inguinal node recurrence after 4 months[26]. Moozar et al. reported that the overall survival after combined modality treatment –surgery radiotherapy and chemotherapy in a Canadian center was 12 months[27]. Our patient received chemotherapy and local radiotherapy to the inguinal nodes and had a good local and systemic control for more than 5 years.

## CONCLUSION

For anorectal malignant melanoma, multimodality treatments including surgery, chemotherapy, and radiotherapy have been used. Surgery is the main treatment. The surgical procedure varies from WLE to APR. Because of nonspecific symptoms, it is easily mistaken for hemorrhoids. Advanced anorectal melanoma most likely represents a systemic disease at time of diagnosis. The prognosis depends on the staging, and it is important to detect anorectal melanoma at an early stage. Therapeutic strategies should be adjusted to the prognosis of the disease. New modalities of medical, biological or immunological therapies have improved the final outcome of these patients.

## CONFLICTS OF INTEREST

No authors have any conflicts of interest or financial ties to disclose.

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**How to cite the article:** Ashok Kumar Diwan, Namita Nangia. Malignant Melanoma –An Exceptional Survival of Five Years. Int J Med Res Prof. 2015, 1(3); 71-75.