Primary Anorectal Melanoma-Uncommon Entity and Rare Presentation

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Abstract: *Background*: Malignant melanomas of the gastrointestinal (GI) tract are usually metastatic. Primary malignant melanoma of the GI tract is rare and occurs mainly in the anorectum and esophagus, but can also involve stomach rarely.

Case: We report a case of 65-year-old female who presented with short duration of anemia but on detailed evaluation had primary Anorectal melanoma (ARM) with extensive metastasis.

Conclusion: An evaluation of short duration of anemia led to unexpected widely metastasized primary anorectal melanoma. Hence anemia presenting at old age should be evaluated in detail including endoscopy of whole gastro-intestinal tract to rule out malignancy.

Keywords: Anemia, Anorectal Melanoma, Endoscopy, Colonoscopy.

INTRODUCTION

Malignant melanomas of the gastrointestinal (GI) tract are usually metastatic. Primary malignant melanoma of the GI tract is rare and occurs in the anorectum and esophagus. Moore described primary malignant melanoma of the anorectum for the first time in 1857. Malignant melanoma of the anorectum (ARM) is an uncommon and highly malignant condition. It represents 0.2%–3% of all malignant melanomas and 0.1%–4.6% of all anorectal tumours. The prognosis of this highly malignant condition is poor. The 5-year survival rate for anorectal melanomas has been reported as less than 20%, compared with a reported mean 5-year survival for cutaneous melanomas of approximately 80% [1]. We report a case of 60-year-old female who presented with short duration of anemia but on detailed evaluation had primary ARM with extensive metastasis.

CASE REPORT

A 65-year-old female presented with short duration history of easy fatiguability, generalized weakness, loss of appetite and mild diffuse colicky abdominal pain for a period of one month. There was no history of alteration of bowel habit, lower GI bleed or rectal mass prolapse. On examination she had pallor, hepato-Splenomegaly and a hard irregular mass felt 4 cm above anal verge arising from posterior wall on per rectal assessment. Her preliminary investigations were significant only for microcytic hypo chromic anemia (Hemoglobin level of 7 gm%) but all rest blood tests including blood sugar, liver function tests, renal function tests, serum carcinoma embryonic antigen (CEA) and alpha–feto protein (AFP) levels, were found to be essentially normal. In view of her old age and anemia being the only presentation, full detailed evaluation was warranted for ruling out any loss from gastro-intestinal tract because at this age malignancy of this site is an important and most commonly missed entity, hence leading to delayed diagnosis. The abdominal ultrasonogram (USG) revealed multiple space occupying lesions (SOL's) in the liver. The computed tomographic (CT) scan showed metastatic SOL's in brain, multiple metastatic pulmonary deposits (Figure **1**), liver SOL's, (Figure **2**) irregular ano-rectal mass (Figure **3**) and few enlarged Para – aortic lymph nodes below left renal hilum. On Colonoscopic examination, large polypoidal anorectal melanotic growths (Figure **4**) with multiple satellite lesions were seen in the duodenum (Figure **5**) and Colon (Figure **6**). The biopsy tissue taken from anal growth, on histopathological sections showed fragments of the squamous mucosa with the sub epithelial tissue infiltrated by the tumor. The latter composed of sheets of polygonal and spindloid cells with scanty cytoplasm, round to oval hyper chromatic nuclei with granular chromatin. Most of the cells were loaded with melanin pigment which was confirmed by Masson's Fontana stain and bleaching methods (Figures **7** & **8**). In view of the above findings diagnosis of primary anorectal melanoma with metastatic malignant melanoma was made. In view of

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E-ISSN: 2312-5411/14

poor prognosis due to the advanced stage of the disease and financial constraints, family members opted against palliative radiation and chemotherapy.

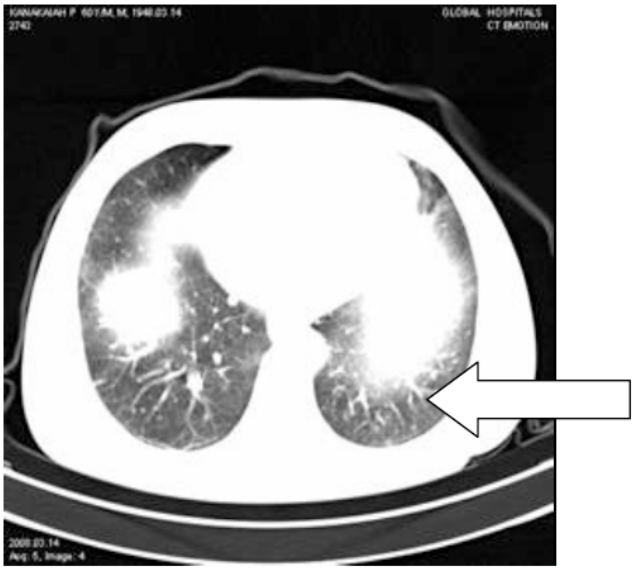

Figure 1: CECT Chest showing Metastatic Pulmonary Deposits.

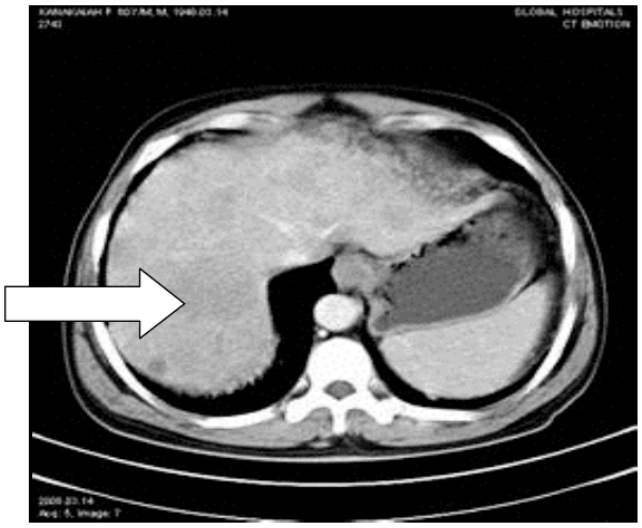

Figure 2: CECT Abdomen (Arterial phase) showing Multiple Liver Metastases.

DISCUSSION

Primary anorectal melanoma comprises 0.25% to 1.25% of all the malignancies originating in this anatomic region. Of all melanomas, anal melanoma represents 0.4% to 1.6% and is the third most common site of origin, following the skin and eye. Mucosal melanomas account for approximately 1.2% of all melanomas, and anorectal melanomas account for fewer than 25% of all mucosal melanomas [2-6]. ARM is usually diagnosed in later decades of life, has slightly female preponderance and rectal bleeding is the main symptom. Unlike cutaneous melanoma, the anorectal melanomas do not have a precursor lesion and do not

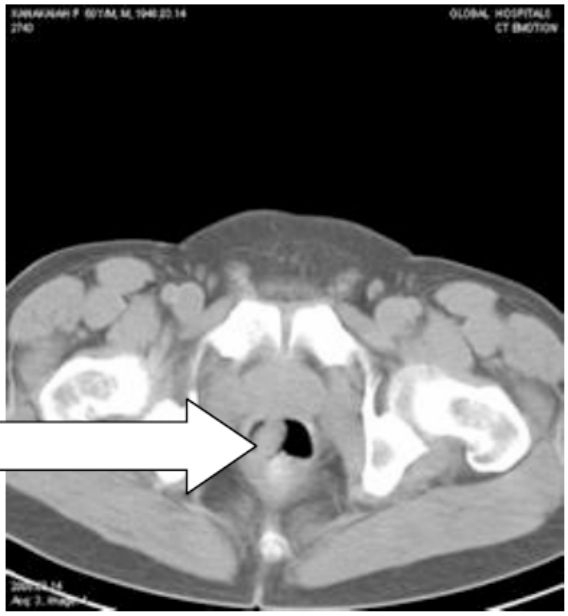

Figure 3: CT Pelvis showing Anorectal Mass.

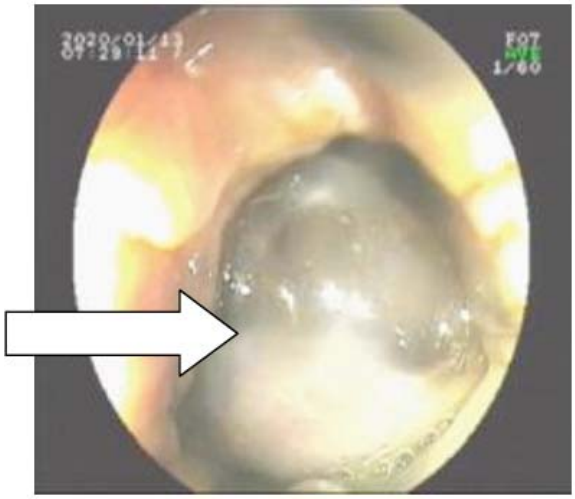

Figure 4: Colonoscopic view of Anorectal Melanoma.

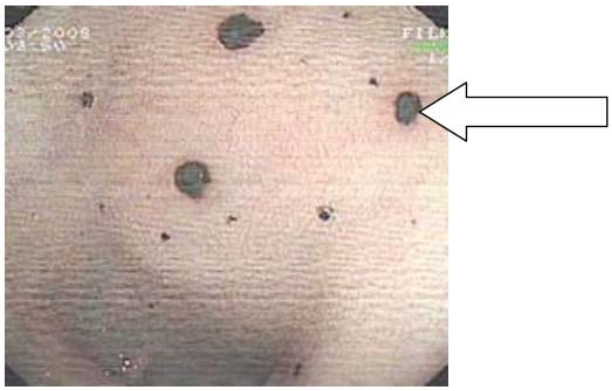

Figure 5: Endoscopic view showing Melanotic Deposits in Duodenum (D1).

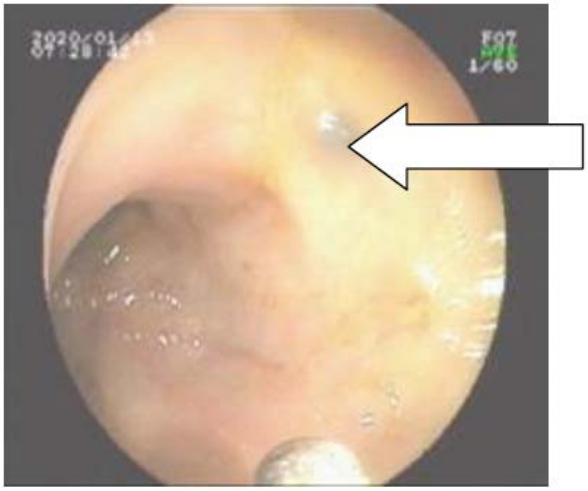

Figure 6: Colonoscopic view showing Melanotic spots in Descending Colon.

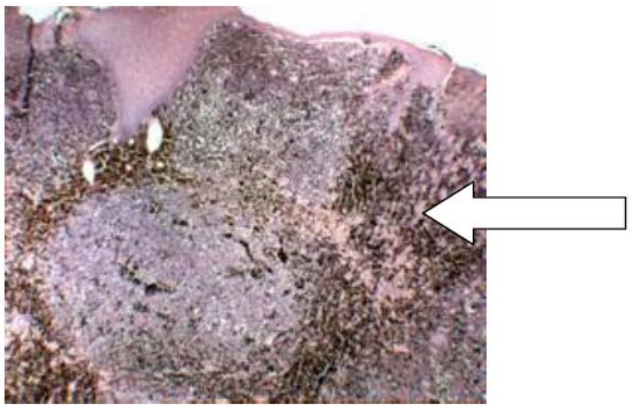

Figure 7: Low Power Histopathological view of Anorectal Melanoma showing Melanin containing Malignant Cells.

relate to ultraviolet exposure. Patients with ARM may complain of anal discomfort, pain, constipation, rectal bleeding, or a protruding mass. The latter may be confused with hemorrhoids, which delay the initial diagnosis [3-7]. The most common presenting symptom is rectal bleeding. Up to 60% of patients have metastatic disease at the time of diagnosis. ARM usually present with early dissemination of disease. The reasons are probably delay in diagnosis and high vascularization of this region [5, 9]. The mean survival time is very short i.e. only 15 months. Only 5 to 10% of patients with ARM will be alive five years after the diagnosis. The prognosis seemed to be related to tumor size and thickness. In most series, none of the patients with a tumor more than 2 mm thick were alive at 5 years. Conversely, sporadic cases with prolonged survival of more than 10 years have been documented. The factor for predicting long term survival is unknown but may be correlated with the initial depth of tumor invasion or with absence of distant metastasis at the time of diagnosis [8].

The epithelial lining of the anal canal is of adenomatous type in the upper part and is squamous in the lower part. The middle zone, also known as the anal transitional zone (ATZ), is characterized by an epithelium which bears resemblance to that of the anal glands, but show little mucus secretion. The melanocytes as demonstrated recently by melanocyte specific antibody (HMB-45) are usually located in the anal squamous zone and not in the colorectal zone, as

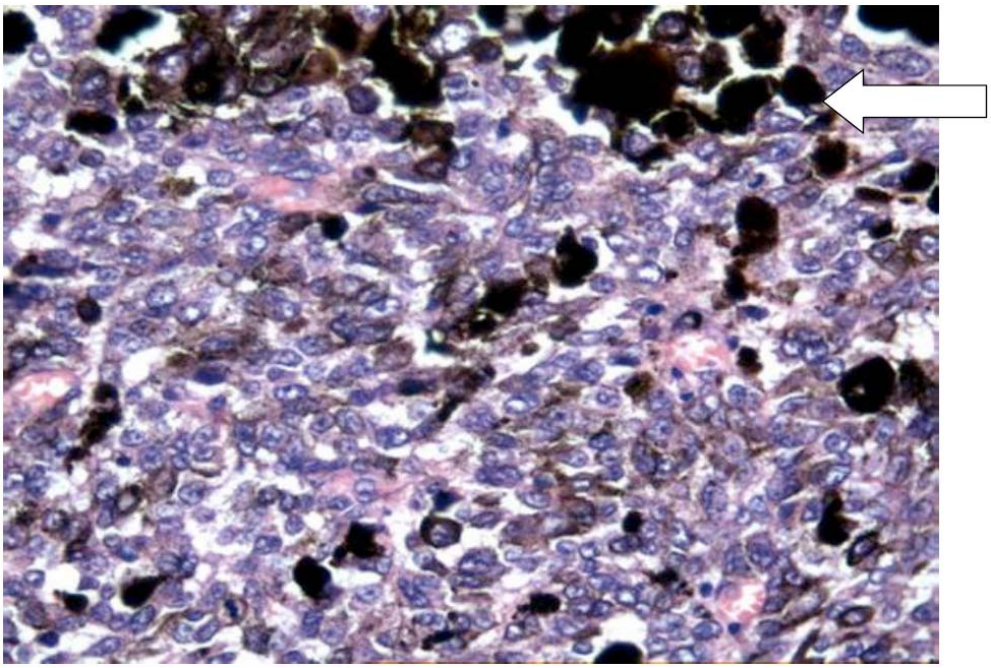

Figure 8: High power histopathological view of Anorectal Melanoma showing Melanin containing Malignant cells.

was thought before. But in tumorous conditions, there is demonstration of melanocytes in all the three zones, which is interpreted as a tumor-induced proliferation of benign melanocytes, which are normally present, but in very small numbers or 'masked'. Thus the demonstration of melanocytes in all three zones of the anal canal substantially supports the observation that malignant melanoma of the anal canal may originate not only below, but also above the dentate line. Macroscopically, the majorities of these tumors are polyploidy and pigmented and arise near the dentate line, as in our patient. It may also present as a nodular prolapsed mass. Once a rectal or anal mass is documented, pigmentation may be one of the clues for the identification of ARM however; macroscopic pigmentation may not always be present. Criteria for primary melanoma include lack of concurrent or previous removal of a melanoma or atypical melanocytic lesion from the skin, lack of other organ involvement, and in situ change in the overlying or adjacent gastrointestinal epithelium. This latter feature, recognized histologically by the presence of atypical melanocytic cells in the basal layer of the epithelium and extending in a "pagetoid" fashion into the more superficial epithelium, may be reported in 40%-100% of primary GI melanomas, as in our case. Tumor cells show varying proportions of spindle cells and epithelioid areas and are frequently cohesive. They may either show abundant melanin pigment or may be completely amelanotic. S-100 has a high sensitivity and HMB-45 has high specificity for diagnosis of melanoma. HMB-45 recognizes a premelanosomal glycoprotein related to the tyrosinase system, and may thus be negative in undifferentiated amelanotic neoplasm.

Primary treatment of malignant anorectal melanoma is surgery [2]. There is controversy regarding the best surgical procedure which ranges from wide local excision (WLE) to abdominoperineal resection (APR). No statistically significant survival advantage has been demonstrated for APR over wide local excision when patients are compared by similar stages [5, 6, 8, 10-12]. Poor prognosis was evident in each series, with a 5-year survival of less than 20%, regardless of the operative method. Surgical decisions must therefore be individualized according to the severity of the local symptoms, prevalence of distant metastases and overall well-being of the patient. Recent reviews advocate sphincter sparing LE, because patients tend to succumb to metastases regardless of surgical therapy. Chemotherapeutic agents including interferon-Alfa, cytokines, biological agents like vaccines, and radiation therapy for brain metastases have been used as adjuvant and palliative therapy for malignant melanoma in general [7, 13, 14].

CONCLUSION

In summary, an evaluation of short duration of anemia led to unexpected widely metastasized anorectal melanoma. Hence anemia presenting at old age should be evaluated in detail including endoscopy of whole gastro-intestinal tract to rule out malignancy. Anorectal melanoma is an unusual cancer that often presents late in its course. Abdominoperineal resection (APR) has not been shown to increase survival in these patients compared with local excision. In advanced cases, local excision may not be feasible without substantial morbidity, and more aggressive surgical therapy like APR is not warranted in presence of metastatic disease. The use of monoclonal antibodies, tumor vaccines, adoptive immunotherapy, and gene therapy aimed at increasing the immunogenicity of these tumors is being studied [15-17].

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Received on 16-05-14 Accepted on 19-05-14 Published on 03-12-2014

DOI: http://dx.doi.org/10.12974/2312-5411.2014.01.02.2