**Case Report:**

**Malignant Melanoma Infiltrating the Bone Marrow**

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**Citation**

Submitted: Mar 29, 2022; Accepted: Apr 18, 2022; Published: Apr 30, 2022

**Abstract:** Malignant melanoma with infiltration into the bone marrow is seldom reported in the literature, for they are exceedingly rare. The primary site is not always apparent and a sizeable number of cases have been attributed to an occult primary. Metastasis to bone marrow is a terminal event usually occurring in stage IV of the disease and can be a focus of residual tumor cells which can cause a relapse. The current documentation is of a case of melanoma occurring as a rectal primary with anemia, thrombocytopenia, and leukoerythroblastic reaction. The marrow aspirates and trephine biopsy showed round to spindle-shaped malignant cells with intracytoplasmic brown-black coarse pigment, suggestive of melanin. The patient was diagnosed with stage IV melanoma but was lost for follow-up. The recognition of such an entity is important for both pathologists and clinicians alike. This case is being reported for the novelty of such an occurrence.

**Key Words:** Malignant melanoma, bone marrow, leukoerythroblastic reaction, melanin

**Introduction:**
The vascular nature of the bone marrow renders it one of the most common sites of hematogenous metastasis of a malignancy. Although the more common entities include prostate, breast, and lung carcinomas, malignant melanoma infiltrating the marrow is exceedingly rare. (1) Malignant melanoma accounts for less than 5% of all malignancies, but an ever-increasing incidence is being reported worldwide. Bone marrow metastasis during the disease is estimated to be 5-7% of cases. (2) Although cases are reported in the literature with a known primary, several cases are also documented amounting to around 5-15%; where an occult primary has been incriminated. (2,3) We herein report a case of melanoma infiltrating the bone marrow from a rectal primary.

A 50-year-old male patient presented with a one-month history of fatigue and lower backache. He also gave a history of weight loss. On examination, the patient was pale. No lymphadenopathy or organomegaly was detected. On per rectal examination, a nodular mass was palpable in the anterior rectal wall. The mass was firm to hard in consistency, non-tender, and fixed to the underlying anal mucosa. On colonoscopic examination, a 3x2cm hyper-pigmented mass was noted with surface ulceration. In the radiological examination by magnetic resonance imaging (MRI), several osteoblastic lesions were noted in the pelvis including a pre-sacral mass. The biopsy of the same was reported as malignant melanoma, showing the malignant cell’s positivity for the HMB-45 marker. On routine blood examination, the complete blood counts of the patient showed the following: hemoglobin 7.6gm%, total leucocyte count of 4200/mm³, platelet count of 110x10^3/mm³. The peripheral blood smear showed sparse erythrocyte distribution with poikilocytosis and few reticulocytes. Occasional nucleated red blood cells were also seen. The biochemical investigations were fairly unremarkable. Given the mild cytopenias and as a part of tumor staging, a bone marrow examination was advised. The bone marrow aspirates showed cellular particles with cell trails diluted by sinusoidal blood. But the smears as well as the imprint smear showed scattered round to spindle-shaped malignant cells with a high nucleus: cytoplasmic ratio, coarse chromat, and a single prominent nucleolus. The cytoplasm of the cells showed brown-black coarse pigment, suggestive of melanin (Figure 1). Cytochemical reactions of these cells were tested with Masson-Fontana, which showed positivity for the granules. Thus, a report of marrow infiltration by malignant melanoma was given.

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OJHAS 2022;21(1):10 Khanna R, Nayak D, Vasudevan G, Singh VK. Malignant Melanoma Infiltrating the Bone Marrow.
The trephine biopsy revealed trabecular bone enclosing cellular marrow showing infiltration by cords and nests of round to spindle-shaped malignant cells, in the interstitium and paratrabecular region. The cells showed moderate to abundant cytoplasm with intracytoplasmic melanin pigment, vesicular to coarse nuclei with a single prominent nucleolus. Few extravasated melanin pigment deposits were also noted. The atrophic stroma showed few preserved hematopoietic elements. These features were consistent with melanoma infiltration.

**Discussion:**

A study of the available literature reveals that a malignant melanoma metastasizing to the bone marrow is exceedingly rare. In a review article published by Jain et al., a prevalence of 7% is reported in antemortem cases and surprisingly perhaps, 45% of autopsy cases. Also, the involvement of the bone marrow in melanoma had a wide age distribution (3-75 years; mean: 51.5) with a normal male to female ratio (1.33:1). (1) In the present case, the demographic of the patient is on similar lines. Bone marrow involvement from primary melanoma in the anorectal region has only rarely been described in the literature. (2) In the present case, the primary tumor was seated in the rectum as a nodular mass. The peripheral blood picture showed anemia and thrombocytopenia with a mild leucoerythroblastic reaction, which has been described in the available literature as well. (2) Other associations with melanoma include findings like anemia, pancytopenia, leukocytosis, splenomegaly, and microangiopathic hemolytic anemia with progression to disseminated intravascular coagulation. (2,4–6)

With around 30 cases reported in English literature till now the metastatic potential of melanoma to bone marrow is underrecognized. Pancytopenia, leukocytosis, hepatosplenomegaly at presentation beckons differentials like lymphomas, while a leucoerythroblastic reaction favors a metastatic solid organ malignancy. In such cases, the morphology of such neoplastic cells portends a peculiar challenge, mandating an ancillary work-up with S100, HMB-45, or Melan-A immunohistochemistry (IHC). (6) Recent strides in the flowcytometric evaluation of bone marrow have led to the characterization of melanoma metastasis in the bone marrow, both in evident deposits in scattered disseminated tumor cells. The metastatic melanoma/disseminated tumor cells showed the most consistent expression of CD56. Other expressed markers include CD57, CD61, CD71 and CD117. (6,7) The classical types of melanomas are well appreciated by their distinctive cytoplasmic melamin pigment. In this case, an IHC study was not performed on the marrow trephine because the primary rectal biopsy had shown a strong positivity for HMB-45, a specific marker for melanoma.

Approximately 40% of melanomas show distant metastasis 4-5 years after the excision of the primary lesion. Involvement of bone marrow places the primary disease into an advanced stage (stage IV), which itself has a bad outlook for the patient. Chernysheva et al., in their flow cytometry-based analysis of bone marrow, demonstrated the presence of disseminated melanoma cells in 57% of cases, with a startling proportion of 26% being seen even in stage I skin melanomas. (7) The presence of these disseminated tumor cells in bone marrow refers to the aggressive nature of even stage I skin melanomas. (7) The presence of these disseminated tumor cells in bone marrow refers to the aggressive nature of even stage I melanomas and provides a basis for the appearance of metastatic disease after the surgical resection of primary. In the present case, the patient was lost to follow-up and at the time of submitting this article, no further details were forthcoming on this case.

**Conclusions:**

A malignant melanoma infiltrating the marrow is exceedingly rare and carries a bad prognosis for the patient. The recognition of such an entity is important for both pathologists and clinicians alike. This case is being reported for the novelty of such an occurrence.

**References:**