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# Beyond Pigment: Amelanotic Melanoma Metastasis To Liver Uncovered By FNAC.

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**ABSTRACT**

Amelanotic melanoma (AM), a subtype of melanoma characterized by the lack or minimal production of melanin pigment poses significant diagnostic challenge due to its atypical appearance. When this elusive cancer metastasizes to liver, its diagnosis becomes even more difficult. In such cases FNAC emerges as a vital tool in aiding clinicians in the accurate diagnosis. This article aims to provide a thorough review of the current literature on the diagnosis of amelanotic melanoma metastasis in the liver using FNAC and cell block

**Keywords:** Amelanotic melanoma, FNAC, metastasis, liver, cell block.

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## INTRODUCTION

Amelanotic melanoma, a variant of malignant melanoma, accounts for approximately 2-8% of all malignant melanoma cases [1]. Unlike typical melanomas, it lacks the characteristic features of pigmentation, making it difficult to diagnose and differentiate from other malignant conditions [2].

Metastasis to the liver signifies an advanced stage of the disease, necessitating accurate diagnosis and prompt intervention [3]. Various studies have highlighted the importance of multimodal imaging approaches, with USG serving as an initial screening tool for detecting liver abnormalities. Ultrasonography (USG) guided Fine Needle Aspiration Cytology (FNAC) with cell block analysis has emerged as a valuable diagnostic tool in this context, aiding in the identification and characterization of liver lesions. We are describing a case of a 30-year-old female diagnosed as amelanotic melanoma metastasize to liver, along with the diagnostic intricacies, challenges, and management strategies associated with this condition through a comprehensive review of literature.

### Case Report with review

A 30-year-old female presented with a 3-month history of progressive abdominal distension, jaundice, and weight loss. The patient was in distress due to abdominal pain and distension. On examination, patient had jaundice and hepatomegaly. USG abdomen showed a large mass lesion in the right lobe of liver. Computed tomography (CT) scan revealed hepatomegaly and multiple hypodense lesions in bilateral lobes showing heterogenous enhancement suggestive of metastasis, mild splenomegaly and metastatic bone lesions with pulmonary metastasis. Considering the presence of mass lesion in liver, USG-guided FNAC of the liver lesion was performed. The cytology smears showed presence of atypical cells arranged in sheets, clusters as well as scattered singly admixed with benign hepatocytes and foamy macrophages against a hemorrhagic background. These atypical cells have high N:C ratio, large pleomorphic nuclei, coarse nuclear chromatin, prominent 1-2 nucleoli and moderate amount of cytoplasm. An extensive panel of IHC markers was applied on the cell blocks prepared to know the primary lesion. These atypical cells were found to be negative for CK, Hep-par 1, CDX2, PLAP, CD20, CA19.9, MUC-1 and positive for vimentin, S100 and HMB-45, ruling out carcinoma, sarcoma, germ cell tumor and lymphoma and establishing the diagnosis of metastatic amelanotic melanoma. Patient was lost to follow up and further work up to know the site of primary tumor could not be done.

## DISCUSSION

Metastatic melanoma is an aggressive tumor which has the potential to metastasize to distant organs, liver being a common site of metastasis, along with the gastrointestinal tract, lungs, brain, bones, and adrenal glands [4]. In a study conducted by Kapatia et al, 51 patients of malignant melanomas or its metastasis were analyzed. Among the metastatic sites, Lymph nodes were found to be the predominant site for metastasis followed by liver. The liver was found to be the most common visceral organ for metastasis of malignant melanoma [5].

In another study conducted on autopsies of a series of melanoma cases by Memorial Sloan Kettering Cancer Center, it was found that malignant melanoma most commonly metastasizes to the liver within the gastrointestinal tract [6]. Hence early detection is the key to reduce mortality rates in affected patients. Integrating FNAC with cell block processing and immunohistochemistry enables precise characterization of challenging lesions, thereby ensuring timely therapeutic intervention and improved patient outcomes. FNAC is a quick, low cost and effective procedure with sensitivity and specificity of 0.97 and 0.99 respectively in diagnosing metastatic melanoma [4, 7]. So it should be the first diagnostic modality when melanoma is suspected.

Diagnosis of amelanotic melanoma relies predominantly on cytomorphological assessment complemented by ancillary techniques like IHC and molecular profiling. Morphologically, amelanotic melanomas exhibit variable patterns, mimicking carcinomas, sarcomas, lymphomas, or undifferentiated round cell neoplasms. Recognition of subtle architectural clues, such as nuclear pleomorphism, prominent nucleoli, irregular chromatin distribution, and occasional mitotic figures, coupled with awareness of clinical history, assists in arriving at a correct interpretation. Ancillary testing adds another layer of confidence. However, the differential diagnosis of lesions can complicate the diagnostic process and a comprehensive approach is required to identify the correct diagnosis. The complexity of diagnosing

melanoma metastases in the liver is well documented. It can present in various patterns on fine needle aspiration such as pleomorphic, spindle cell, myxoid, lymphomatous, anaplastic and clear cell type [8]. Melanin pigment in the tumor cell cytoplasm usually diagnostic of melanoma, when absent poses a diagnostic dilemma.

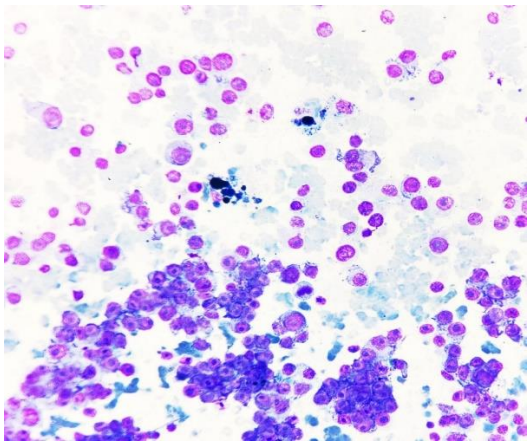

**Figure 1: Leishman-Stained Smear (At Low Power) Showing Atypical Cells In Groups And Scattered Singly In A Hemorrhagic Background.**

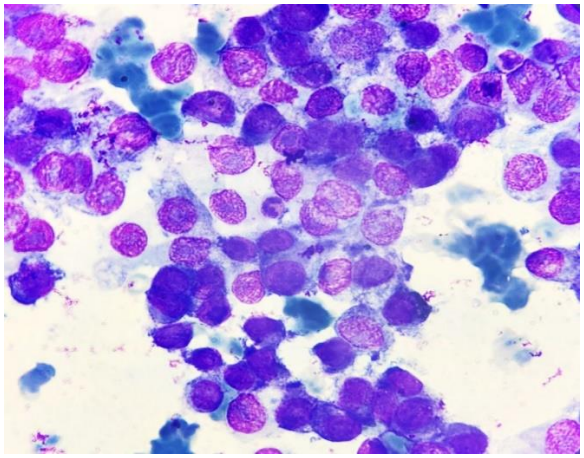

**Figure 2a**

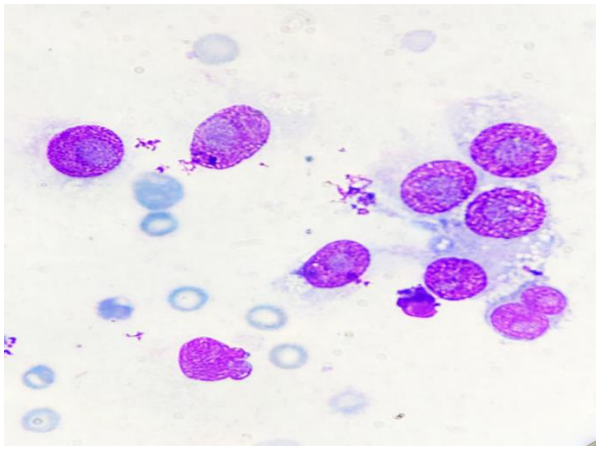

**Figure 2b**

**Figure 2a and 2b: High Power View Of Leishman Stained Smear Showing Atypical Cells With High N:C Ratio, Coarse Chromatin And Prominent Nucleoli.**

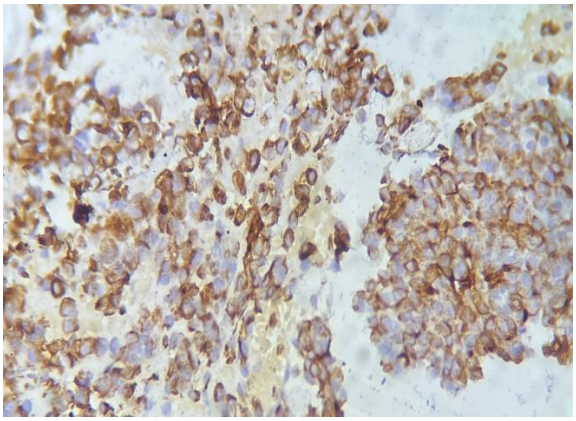

**Figure 3: IHC- Vimentin Showing Membranous Positivity.**

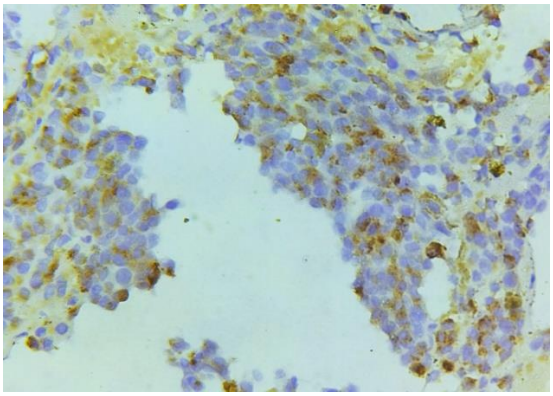

**Figure 4: IHC HMB -45 Showing Cytoplasmic Positivity**

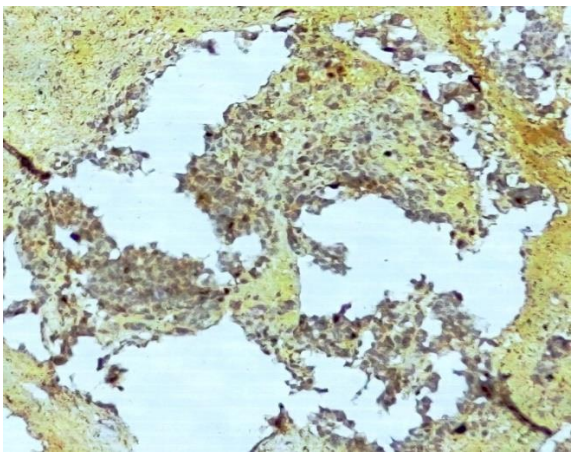

**Figure 5: IHC S100 Showing Nuclear And Cytoplasmic Positivity In Atypical Cells.**

In our case also, the malignant cells morphology is not diagnostic of any specific carcinoma as well as there were no granules in tumor cells. Hence it was treated as metastasis from unknown primary and all possible malignancies were ruled out using a panel of immunohistochemistry markers on cell block. Vimentin, S-100 and HMB 45 came out to be positive establishing the diagnosis of amelanotic melanoma.

Another case report by Tokuhara et al details the first case of metastatic anorectal melanoma with liver metastases and metastasis to the right ischium, highlighting that metastases can occur at multiple sites simultaneously [9]. Although the medical literature is conflicting, the prognosis for metastatic melanoma with an unknown primary tumor is thought to be similar to that of melanoma with a known primary tumor [3]. Metastatic melanoma of unknown primary tumor was first described by Das Gupta et al in 1963 [10].

Subsequent studies showed that 2% to 6% of patients with malignant melanoma are comprised of metastatic tumors of unknown primary tumor group. It is believed that 10-15% of these patients have malignant melanoma [11, 12].

The American Joint Committee on Cancer (AJCC) has begun a review of metastatic melanoma cases divided into three subgroups. Malignant melanomas with skin, subcutaneous tissue, or distant lymph node metastases were classified as M1a. Cases with lung metastases were classified as M1b, and metastases to other solid organs were classified as M1c. Patients with stage M1a have a life expectancy of 10 to 18 months. According to the AJCC classification, the M1c stage is different from M1a and M1b [13].

The most common organs that melanoma usually metastasizes to are the brain, gastrointestinal tract, and liver, respectively. The average life expectancy for malignant melanoma with metastases to the gastrointestinal tract or liver is approximately 6 to 9 months. This proportion exceeds 46–48 months after definitive surgery [14]. Although metastatic melanoma has a very poor prognosis, recent studies have shown that definitive surgical treatment combined with chemoradiotherapy can significantly increase life expectancy in these patients [15].

## CONCLUSION

Amelanotic melanoma metastasis to the liver diagnosed via FNAC represents a complex clinical scenario requiring meticulous evaluation and multidisciplinary management. While FNAC offers a minimally invasive approach to tissue sampling and cytological analysis, its diagnostic accuracy hinges on various factors, including sample adequacy, interpretation expertise, and ancillary testing. Continued research and clinical experience are essential for refining diagnostic algorithms and therapeutic strategies in the management of metastatic melanoma.

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