EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 11
Issue: 4
161-166
Year: 2024

A RARE CASE OF AMELANOTIC MELANOMA OF THE LEFT FOOT WITH LEFT INGUINAL LYMPH NODE METASTASIS

Bhumika Patel*[1], Jagadale Kunda[1], N. S. Mani[1], Mahendra Chaudhari, M.D.[2], Sai Sankeerth Madakasira, M.D.[2] and Anish Jagadale[3]

[1]Bharati Vidyapeeth, Deemed to be University Medical College, Pune, Maharashtra, India.
[2]Graduate Medical Sciences (GMS) Division of Boston University Chobanian & Avedisian School of Medicine on the Boston University Medical Campus, Boston, Massachusetts, USA.
[3]B J Government Medical College Jai Prakash Narayan Road, Railway Station Rd, Pune, Maharashtra, India.

***Corresponding Author: Bhumika Patel**
Bharati Vidyapeeth, Deemed to be University Medical College, Pune, Maharashtra, India.

Article Received on 04/02/2024 **Article Revised on 24/02/2024** **Article Accepted on 14/03/2024**

ABSTRACT

Introduction: Presence of melanin pigment allows for diagnosis of malignant melanoma. However, amelanotic melanomas make up 2 to 20% of all melanomas which contain little or no pigment. So, use of Immunohistochemistry (IHC) in diagnosis of amelanotic melanoma is essential. **Case presentation**: A 31-year-old female patient presented with a left foot ulcer since 10 years and left inguinal swelling since 6 months. Fine Needle Aspiration Cytology of Left inguinal lymph node was suspicious for malignancy. No pigments were found in left foot ulcer biopsy and left inguinal lymph node(s). A pre-emptive diagnosis based on biopsy was a poorly differential malignancy with inguinal metastatic deposits. Upon performing Immunohistochemistry with one melanocytic marker diagnosis was established as amelanotic melanoma. **Discussion:** Amelanotic melanomas have no cytoplasmic melanin pigment. They have one or more secondary amelanotic lesions. There is no distinctive morphological look. It is hence advised to rule out amelanotic melanoma in every poorly differentiated tumour using Immunohistochemistry markers like Melan A and HMB45. The most sensitive marker, S100 is 95–100% positive in melanomas. **Conclusion:** When a diagnosis of poorly differentiated malignancy is obtained, performing melanotic markers in the immunohistochemistry panel must be considered to confirm or rule out amelanotic melanoma.

KEYWORDS: Amelanotic Melanoma, Histopathology, Immunohistochemistry, Melanoma, Melanotic markers.

INTRODUCTION

Melanoma develops from the melanocytes that are naturally present in the skin, mucosa, and other internal organs. On visual or histological investigation, amelanotic malignant melanoma is a subtype of melanoma that contains little or no pigment. Malignant melanoma can be diagnosed without difficulty if melanin pigment is present, however amelanotic melanomas, which make up for 2 to 20% of all melanomas, are notorious mimickers and present a significant diagnostic challenge.[1]

Amelanotic melanomas contain little or no melanin pigment in cytoplasm of tumor cells and may not display characteristic appearance, thus posing diagnostic dilemma. Metastatic melanoma often presents with one or more amelanotic secondary lesions even when the primary tumor was pigmented.[2]

CASE PRESENTATION

A female patient in her early 30s presented with a left foot ulcer and left inguinal lymph node swelling since 6 months. Patient also has history of ulcer at same site, which was operated on 10 years ago.

X-ray of left foot on presentation, consistent with clinical examination, shows soft tissue swelling over 2nd and 3rd toes. Ultra-Sonogram (USG) of soft tissue areas in the left inguinal region showed: multiple, enlarged, hypoechoic lymph nodes in left external iliac and left inguinal region with areas of necrosis.

Fine Needle Aspiration Cytology (FNAC) of left inguinal lymph node revealed degenerated cohesive clusters and few loosely scattered cells with mildly enlarged hyperchromatic pleomorphic nuclei and moderate amount of cytoplasm on the back ground of plenty of neutrophils, lymphocytes and histiocytes. (Figure 1, 2)

Pathologists' final impression was considered for "suspicion of malignancy".

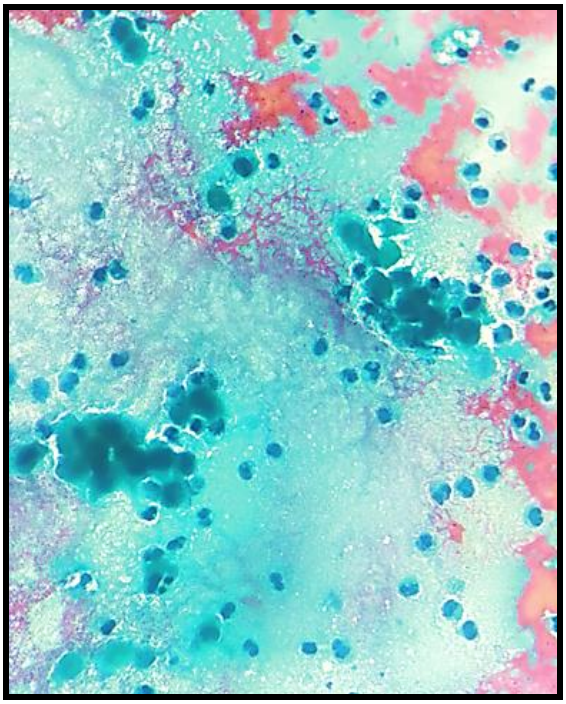

Figure 1: Papanicolaou (PAP) stain of Lymph Node FNAC.

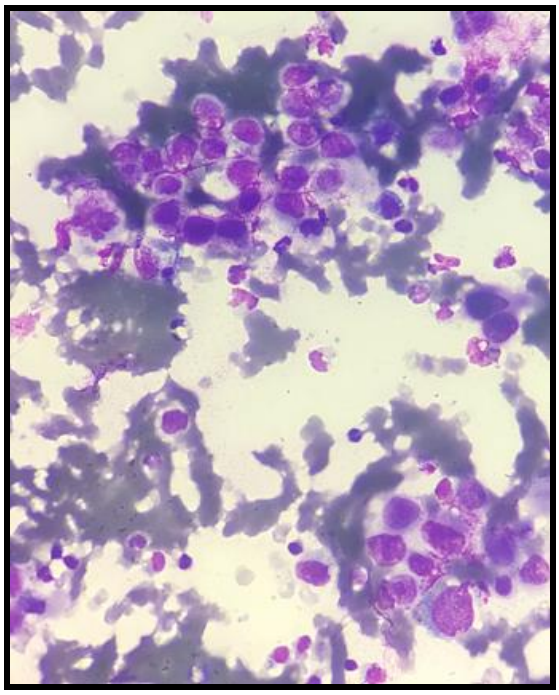

Figure 2: Leishman stain of Lymph Node FNAC.

Histopathological (H&E) examination of Left foot ulcer biopsy showed small round cell arranged in lobules and clusters infiltrating into dermis and sub cutis. Tumor cells are moderate in size and showed mild to moderate pleomorphic hyperchromatic nuclei with prominent nucleoli. Cytoplasm is amphophilic. Cells show spindling at many areas. No pigment was noted. Deeper area showed extensive necrosis. No acinar/squamous differentiation was seen. (Figure 3, 4) H&E based diagnosis was impressed as a "Poorly differentiated malignancy".

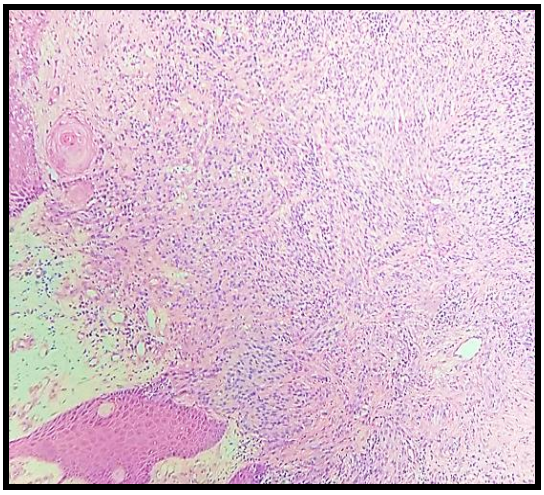

Figure 3: Low power of foot ulcer biopsy H&E.

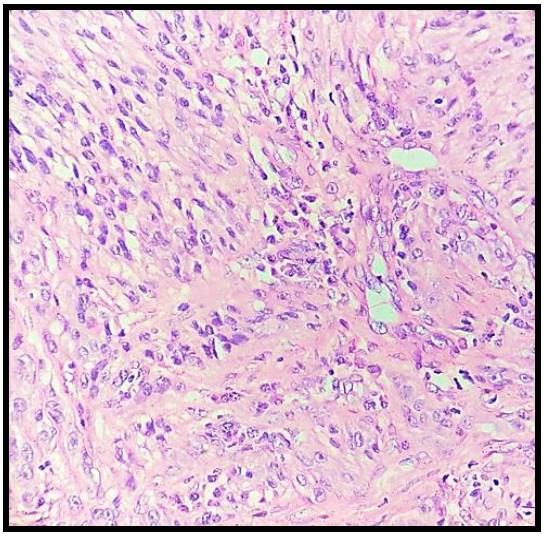

Figure 4: High power of foot ulcer biopsy H&E.

A section of Left inguinal lymph node showed extensive necrosis with acute inflammation along with few small clusters of poorly differentiated polygonal cells showing nuclear atypia.

To further categorize the tumor, Immunohistochemistry (IHC) markers were used comprising of Pan Cytokeratin (CK), CD45, S-100, Desmin and Melan A. The tumor cells were found positive for Melan A and S100. (Figure 5, 6, 7, 8).

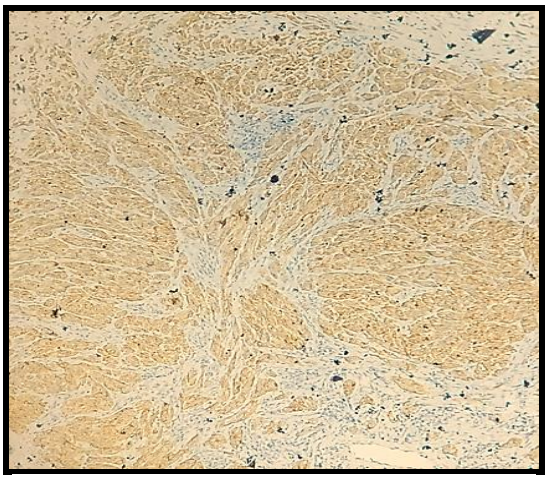

Figure 5: Low power of IHC marker Melan-A

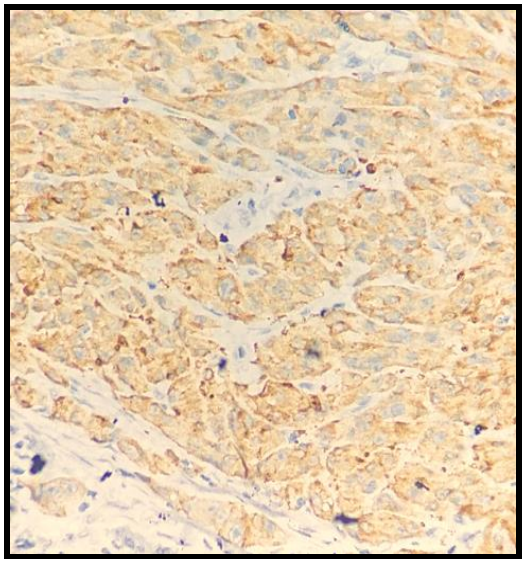

Figure 5: High power of IHC marker Melan-A.

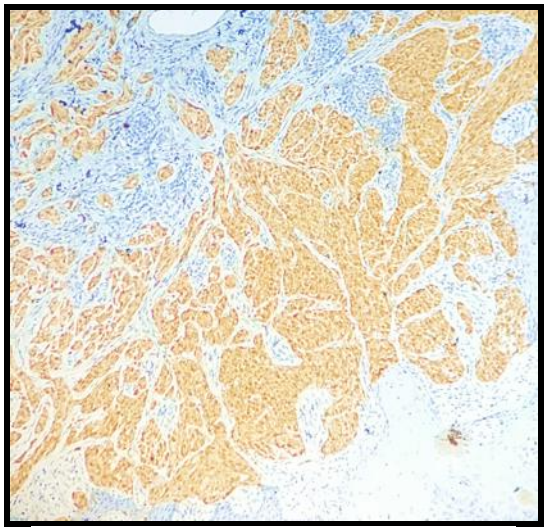

Figure 7: Low power of IHC marker S100.

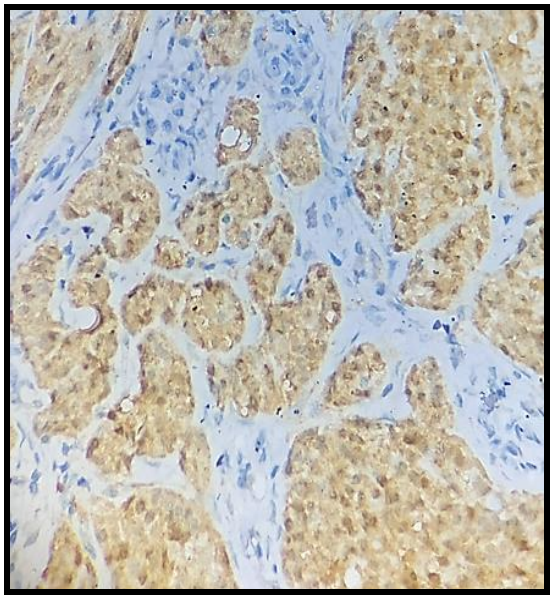

Figure 8: High power of IHC marker S100.

DISCUSSION

Malignant melanomas most commonly occur on skin (over 90%) and less commonly on mucosal surfaces (slightly over 1%). It accounts for approximately 4% of all skin cancers, but accounts for 79% of all skin cancer related deaths.[3] Amelanotic melanoma usually occurs in sun-exposed skin as seen in this particular case.

Cytologically, a high cell yield with a predominant population of dissociated cells, showing nuclear pleomorphism, prominent nucleoli and increased mitotic activity are noted. However, diagnosis of the amelanotic variant on cytology is challenging because of the absence of pigment, the tumor cells mimic those of carcinoma or sarcoma, as seen in this particular case.[4]

Even on H&E, melanoma has attained diagnostic notoriety for its capacity for histomorphological diversity and ability to masquerade as a number of non-melanocytic neoplasms, especially true for the amelanotic variety.[5] Histopathological examination alone, as in this case can leave the pathologist with an extensive list of differential diagnoses as sarcomas, carcinomas, lymphomas.

This case was negative for PanCK, CD45 and desmin. Positive for S-100 and strongly positive for MelanA. S-100 immunomarker is the most sensitive marker and is found to be positive in approximately 95 to 100% of primary mucosal melanomas as compared with 86 and 84% with HMB-45 and Melan-A immunostaining, respectively.[6,7]

Strong positivity of melanocytic marker like Melan A, S100 and histomorphology helped us to a diagnosis of amelanotic melanoma, similar to studies of Limketkai B *et al*, Roy *et al*. and Oguri *et al*.[8,9,10]

This case does not reveal a few features typical of a melanoma such as presence of melanin pigment, junctional activity, grooves and pseudo inclusions. Cells were however showing nuclear pleomorphism, vesicular to hyperchromatic nuclei with prominent nucleoli. Many hypotheses have been proposed to explain the lack of pigment in amelanotic melanoma such as lack of tyrosinase, agenesis of melanosomes, undetectable levels of melanin production or abnormal melanogenesis.[11]

Treatment is wide surgical excision in combination with chemotherapy and to a lesser extent immunotherapy and radiation, with a check on nodal status.[3]

CONCLUSION

Amelanotic melanoma can have a very deceptive clinical presentation. The aim of this case report is to highlight the possibility of amelanotic melanoma when a diagnosis of poorly differentiated round cell tumor is made. Including one melanotic marker in the IHC panel will prevent diagnostic delay. As early detection is the main stay of therapy and aiding in better patient management, this should be an important consideration.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

REFERENCES

1. Thomas, N. E., Kricker, A., Waxweiler, W. T., Dillon, P. M., Busman, K. J., From, L., Groben, P. A., Armstrong, B. K., Anton-Culver, H., Gruber, S. B., Marrett, L. D., Gallagher, R. P., Zanetti, R., Rosso, S., Dwyer, T., Venn, A., Kanetsky, P. A., Orlow, I., Paine, S., Ollila, D. W., … Genes, Environment, and Melanoma (GEM) Study Group Comparison of clinicopathologic features and survival of histopathologically amelanotic and pigmented melanomas: a population-based study. JAMA dermatology, 2014; 150(12): 1306–1314. https://doi.org/10.1001/jamadermatol.2014. 1348.
2. Koch, S. E., & Lange, J. R. Amelanotic melanoma: the great masquerader. Journal of the American Academy of Dermatology, 2000; 42(5 Pt 1): 731–734. https://doi.org/10.1067/mjd.2000.103981.
3. Pandiar, D., Basheer, S., Shameena, P. M., Sudha, S., & Dhana, L. J. Amelanotic melanoma masquerading as a granular cell lesion. Case reports in dentistry, 2013; 924573. https://doi.org/10.1155/2013/924573
4. Siddaraju N. Ming Yu Cao Dr, editor. Clinical Cytology in the Diagnosis and Management of Melanoma, Current Management of Malignant Melanoma, 2011. [Last accessed on 2014 Sep]. ISBN: 978-953-307-264-7, InTech, DOI: 10.5772/18114
5. Shetty, A., Kumar, S. A., Geethamani, V., & Rehan, M. Amelanotic melanoma masquerading as a superficial small round cell tumor: a diagnostic challenge. *Indian journal of dermatology*, 2014; *59*(6): 631. https://doi.org/10.4103/0019-5154.143569.
6. Yu, C. H., Chen, H. H., Liu, C. M., Jeng, Y. M., Wang, J. T., Wang, Y. P., Liu, B. Y., Sun, A., & Chiang, C. P. HMB-45 may be a more sensitive maker than S-100 or Melan-A for immunohistochemical diagnosis of primary oral and nasal mucosal melanomas. Journal of oral pathology & medicine: official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology, 2005; 34(9): 540–545. https://doi.org/10.1111/j.1600-0714.2005.00340.x

7. Blessing, K., Sanders, D. S., & Grant, J. J. Comparison of immunohistochemical staining of the novel antibody melan-A with S100 protein and HMB-45 in malignant melanoma and melanoma variants. Histopathology, 1998; 32(2): 139–146. https://doi.org/10.1046/j.1365-2559.1998.00312.x
8. Limketkai, B. N., Chandrasekhara, V., & Milligan, F. Primary Anorectal Amelanotic Melanoma Presenting as Internal Hemorrhoids. Gastroenterology & hepatology, 5(7): 516–518.
9. Roy, S., Dhingra, K., Mandal, S., & Khurana, N. Unusual presentation of metastatic amelanotic melanoma of unknown primary origin as a solitary breast lump. Melanoma research, 2008; 18(6): 447–450. https://doi.org/10.1097/CMR.0b013e328317f04b
10. Oguri, H., Izumiya, C., Maeda, N., Fukaya, T., & Moriki, T. A primary amelanotic melanoma of the vagina, diagnosed by immunohistochemical staining with HMB-45, which recurred as a pigmented melanoma. Journal of clinical pathology, 2004; 57(9): 986–988. https://doi.org/10.1136/jcp.2004.016220
11. Nalamwar, R., Kharkar, V., Mahajan, S., Chikhalkar, S., & Khopkar, U. Nodular amelanotic melanoma. Indian journal of dermatology, venereology and leprology, 2010; 76(3): 273–275. https://doi.org/10.4103/0378-6323.62972.