Case Report

DOI: 10.7860/JCDR/2022/55869.16570

Pathology Section

Malignant Melanoma Presenting as Multiple Lytic Bone Lesions Masquerading as Carcinoma of Unknown Primary on Clinical and Histopathological Examination

RENU SUKUMARAN[1], LAKSHMI HARIDAS[2], VENUGOPAL MURALEEDHARAN[3]

ABSTRACT

Malignant melanomas are aggressive tumours with frequent metastasis to lymph nodes and viscera. However, patients presenting with osseous metastasis of melanoma with no known primary source is relatively rare. The terminology "metastases of unknown origin" is used when the site of the primary neoplasm cannot be identified at the time of diagnosis despite a thorough history, physical examination, appropriate laboratory testing and imaging studies. Metastatic melanoma can have varied presentations. Herein, authors presents a case report of a 63-year-old female who presented with swelling in the occipital region for eight-month duration. Examination showed bony hard fixed swellings in the occipital and mastoid regions. Computerised Tomography scan (CT scan) showed lytic bone destruction in the occipital and mastoid part of right temporal bone, associated with soft tissue mass. With the differential diagnosis of metastatic carcinoma and myeloma, biopsy was taken which showed infiltrating neoplasm with plasmacytoid cells in cords and in vague nests surrounded by fibrosis. The neoplastic cells were Cytokeratin negative, Cluster of Differentiation (CD) 138 negative and showed patchy nuclear positivity for S100. On subsequent examination, the neoplastic cells showed diffuse strong positivity for Human Melanoma Black 45 (HMB45) and patchy moderate positivity for Melan A confirming the diagnosis of malignant melanoma. Primary lesion could not be detected even after a detailed past medical and surgical history, physical examination and radiological investigations. The main causes of skull lytic lesions in adults are metastatic carcinoma and plasma cell myeloma. Possibility of metastatic melanoma should also be considered in cases of skull bone lesions as melanomas could exhibit varying cellular morphology mimicking carcinoma, sarcoma or haematolymphoid neoplasms.

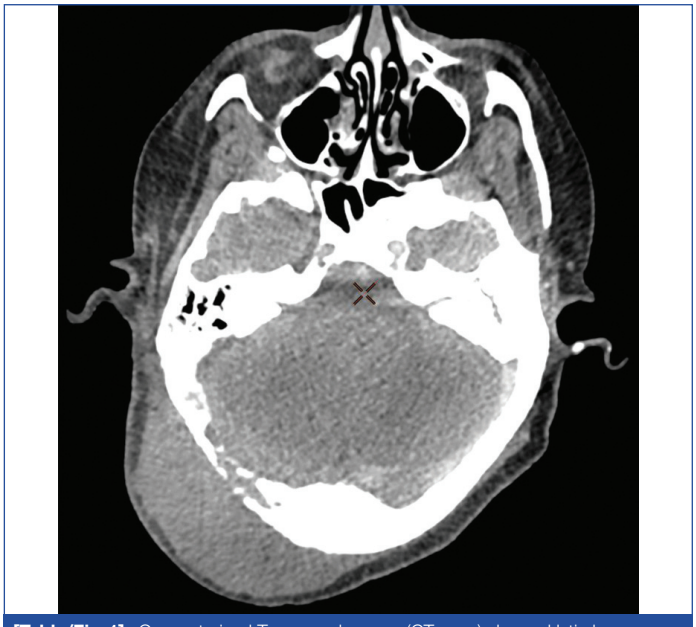
Keywords: Melanoma of unknown primary, Plasmacytoid cells, Skull lesions

CASE REPORT

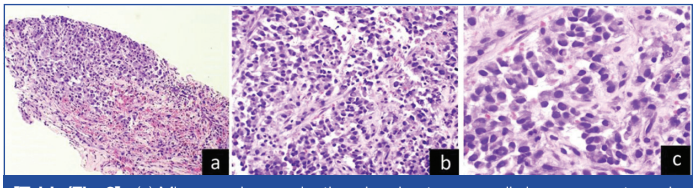
A 63-year-old female presented to regional cancer centre with swelling in the occipital region for eight-month duration with rapid increase in size in past two months, associated with pain. She gave history of diffuse bone pain of two-year duration. Clinical examination showed bony hard, fixed, and tender swelling in the occipital and mastoid regions, measuring 11×10 cm and 5×4 cm, respectively. CT scan showed lytic bone destruction in the occipital and mastoid part of right temporal bone with periosteal reaction, associated with soft tissue mass extending to extra-axial space inwards and to scalp outwards [Table/Fig-1].

Lysis of pterygoid plate along with lytic lesion in manubrium sternum was also noted. Multiple lytic lesions pointed towards the differential diagnosis of metastatic carcinoma and plasma cell myeloma. Biopsy of the lesion was done. Microscopy showed infiltrating neoplasm composed of atypical cells in cords and in vague nests- surrounded by fibrosis. Individual cells were plasmacytoid with moderate amount of cytoplasm, eccentrically placed round/irregular nuclei with variably prominent nucleoli [Table/Fig-2a-c].

With morphological differential diagnosis of metastatic carcinoma and plasma cell myeloma, Immunohistochemical (IHC) examination was carried out. Cytokeratin and CD 138 were negative ruling out the two possibilities. Next panel included S100 with the differential diagnosis of malignant melanoma, which showed patchy nuclear positivity. On subsequent examination, the neoplastic cells showed diffuse strong positivity for HMB 45 and patchy moderate positivity for Melan A confirming the diagnosis of malignant melanoma [Table/Fig-3a-c]. Primary lesion could not be detected even after a detailed past medical and surgical history, physical examination and radiological investigations. Detailed history was taken regarding skin

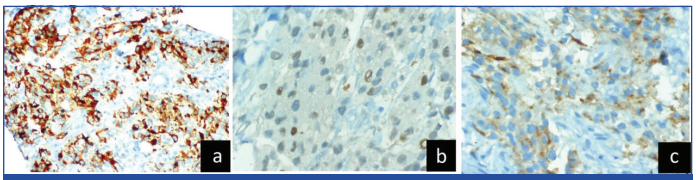


[Table/Fig-1]: Computerised Tomography scan (CT scan) showed lytic bone destruction in the occipital and mastoid part of right temporal bone, associated with soft tissue mass.



[Table/Fig-2]: (a) Microscopic examination showing tumour cells in vague nests and cords (H&E, X50), (b) Plasmacytoid cells (H&E, X200), (c) Higher magnification showing cells with moderate amount of cytoplasm, eccentrically placed nuclei (H&E, X400).

lesions, pigmentation at mucosal sites or any surgical interventions for skin lesions.



[Table/Fig-3]: (a) Tumour cells showing diffuse strong positivity for HMB 45, (b) Patchy nuclear positivity for S100, (c) Patchy moderate positivity for Melan A (IHC, X400).

DISCUSSION

Melanoma of Unknown Primary (MUP) accounts for upto 3% of all melanomas and is defined as histologically confirmed melanoma metastasis to lymph nodes, subcutaneous tissue, or visceral sites without any evidence of a primary cutaneous, ocular, or mucosal melanoma [1,2]. Osseous metastases from malignant melanoma occur in patients with more advanced primary lesions. They are most frequently osteolytic and located in the axial skeleton [2-4]. The wide range of clinical presentations and histopathological patterns of malignant melanoma create diagnostic challenges both for clinicians and pathologists. The clinical diagnosis can be difficult when the lesion occur in an unusual site, present in a metastatic site with an unknown primary or present as non pigmented lesion.

Microscopically these tumour cells can show varied patterns (sheets, cords, trabeculae, pseudopapillary, cords) as well as a variety of histological cell types (spindle, epithelioid, signet-ring cell, pleomorphic, round cell) which may resemble a sarcoma, carcinoma or haematopoietic malignancy. Diagnosis will be more challenging in amelanotic lesions [5-7]. In their study of MUP, Dasgupta TK and Brasfield RD used certain criteria for inclusion-1) absence of history of excision of any skin or anal lesion, 2) a negative ophthalmologic and dermatologic clinical examination, and 3) an absence of scars in the region of affected draining nodal basin [8]. Proposed theories to explain the absence of a primary lesion in MUP include;

1) spontaneous regression of the primary lesion due to immune mechanisms,
2) de novo origin of melanomas in tissues lacking melanocytes and,
3) unrecognised primary lesion [2,3].

The most commonly reported and most feasible explanation for the phenomenon of MUP is the spontaneous regression theory due to immune mechanisms. The same immune mechanisms may be responsible for the slightly better outcomes of patients with MUP, when compared to metastatic melanoma with a known primary of a similar stage [3,6,9,10]. Proper clinical history, physical examination, imaging studies are needed to diagnose MUP. Evaluation of patients suspected to have MUP includes imaging such as CT or 18-Fluorodeoxyglucose-Positron Emission Tomography (18-FDG-PET) scanning to determine the extent of metastatic disease.

The problems encountered in the current case were the unusual presentation, absence of primary lesion, no known clinical or surgical history, amelanotic lesion histologically mimicking carcinoma.

CONCLUSION(S)

When a patient presents with bone metastasis of an unknown primary site, the possibility of metastatic malignant melanoma should also be listed in the differential diagnosis. Melanomas could exhibit varying cellular morphology, mimicking poorly differentiated carcinoma, sarcoma or haematopoietic malignancies. Diagnosis of malignant melanoma may provide a challenge when the primary is unknown, when it occurs in an uncommon location or when exhibits unusual histomorphology, especially in amelanotic lesions.

REFERENCES

[1] Shenoy AS, Desai HM, Kavishwar VS, Savant HV. Metastatic malignant melanoma in a young adult with unknown primary. Indian J Cancer. 2015;52:446-47.
[2] Kamposioras K, Pentheroudakis G, Pectasides D, Pavlidis N. Malignant melanoma of unknown primary site. To make the long story short. A systematic review of the literature. Crit Rev Oncol Hematol. 2011;78:112-26.
[3] Bankar S, Patkar S, Desai S, Shrikhande SV. Unusual presentation of melanoma of unknown primary origin: A case report and review of literature. J Cancer Res Ther. 2015;11:1025.
[4] Phan MB, Phan J, Nguyen C, He J, Nguyen QD. Melanoma with an unknown primary in an asymptomatic elderly male with unilateral lymphadenopathy. Cureus. 2021;13(5):e15140.
[5] Gambichler T, Chatzipantazi M, Schröter U, Stockfleth E, Gedik C. Patients with melanoma of unknown primary show better outcome under immune checkpoint inhibitor therapy than patients with known primary: Preliminary results. Oncoimmunology. 2019;8:e1677139.
[6] van der Ploeg AP, Haydu LE, Spillane AJ, Scolyer RA, Quinn MJ, Saw RP, et al. Melanoma patients with an unknown primary tumor site have a better outcome than those with a known primary following therapeutic lymph node dissection for macroscopic (clinically palpable) nodal disease. Ann Surg Oncol. 2014;21:3108-16.
[7] Premalatha P, Renuka VI, Prasanna Kumar JT, Reddy TR, Tejaswini V, Vahini G. Melanoma masquerading as primary lesion in unusual sites. Arch Int Surg. 2015;5:167-70.
[8] Dasgupta TK, Brasfield RD. Metastatic melanoma of the gastrointestinal tract. Arch Surg. 1964;88:969-73.
[9] Vijuk G, Coates AS. Survival of patients with visceral metastatic melanoma from an occult primary lesion: A retrospective matched cohort study. Ann Oncol. 1998;9:419-22.
[10] Cormier JN, Xing Y, Feng L, Huang X, Davidson L, Gershenwald JE, et al. Metastatic melanoma to lymph nodes in patients with unknown primary sites. Cancer. 2006;106:2012-20.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Pathology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India.
2. Associate Professor, Department of Medical Oncology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India.
3. Professor, Department of Imageology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Renu Sukumaran,
Associate Professor, Department of Pathology, Regional Cancer Centre,
Thiruvananthapuram, Kerala, India.
E-mail: renu.sukumaran@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 01, 2022
- Manual Googling: Apr 23, 2022
- iThenticate Software: Apr 26, 2022 (19%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Feb 23, 2022**
Date of Peer Review: **Mar 30, 2022**
Date of Acceptance: **May 06, 2022**
Date of Publishing: **Jul 01, 2022**