

Nodular Malignant Melanoma Presenting as a Rapidly Growing Pigmented Skin Lesion: A Case Report

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ABSTRACT

Nodular variant of malignant melanoma is a highly aggressive neoplasm arising from melanocytes, accounting for the majority of skin cancer related deaths despite its relatively low incidence. Hereby, the authors present a case of a 68-year-old male patient presented with 10 months history of pigmented nodule with ulceration over left supraclavicular region which gradually increasing in size. There was no any positive family history of similar lesion. Routine haematological and biochemical reports did not show any significant abnormality. Contrast-enhanced Computed Tomography (CT) scan of the thorax revealed a well-defined irregularly marginated heterogeneously enhancing soft-tissue lesion measuring 2.7×1.7×1.6 cm approximately involving left supraclavicular region. For the present particular case, the patient did not undergo prior biopsy procedure. Patient had a wide local excision and condition was determined to be nodular type of malignant melanoma after histopathological examination. Histopathological examination showed high breslow thickness, microsatellitosis, tumour infiltrating lymphocytes, high mitotic rate, focal regression. In the absence of histological confirmation of distant metastasis, the pathological primary tumour category was assigned as pT4b based on the primary tumour characteristics. Following surgical excision, the patient was referred to a tertiary oncology centre for B-Raf proto-oncogene, serine/threonine kinase (BRAF) V600 mutation testing and further oncological management. Given the high-risk pathological features, adjuvant anti-PD-1 immunotherapy was considered. As Nodular Malignant Melanoma (NMM) is a malignant neoplasia with high rate of mortality and bad prognosis, prompt diagnosis is paramount for physicians to start an aggressive treatment. The present case showed the highly aggressive nature of NMM demonstrating multiple adverse prognostic features.

Keywords: Nodular melanoma, Primary tumour, Skin cancer

CASE REPORT

A 68-year-old male presented to the Surgical Outpatient Department (OPD) with a pigmented nodule with ulceration over left supraclavicular region since 10 months. The lesion had gradually increased in size and was associated with occasional itching. There was no history of trauma or previous skin lesions at the site. Patient did not take any medication.

On physical examination, a solitary, dark brown to black nodular lesion measuring 2.7×1.7 cm was noted over left supraclavicular region. The surface was irregular with focal ulceration. The lesion was firm in consistency and non tender. Routine haematological test like Complete Blood Count (CBC), and biochemical investigations like Lactate Dehydrogenase (LDH), Alkaline Phosphatase (ALP) and Serum Glutamic-Pyruvic Transaminase (SGPT), Serum Glutamic-Oxaloacetic Transaminase (SGOT), total bilirubin, total protein, Serum cholesterol, triglyceride, urea, creatinine, uric acid were within normal limits.

Contrast-enhanced CT scan of the thorax revealed a well-defined irregularly marginated heterogeneously enhancing soft-tissue lesion measuring approximately 2.7×1.7×1.6 cm involving left supraclavicular region suggestive of primary cutaneous malignant lesion. Multiple subcentimetric enhancing lymph nodes noted involving pre tracheal, para tracheal, aorto pulmonary, pre vascular and left axillary region. Multiple lytic destructive lesions involving the C3 and C4 vertebral bodies, with cortical destruction were noted suggestive of osseous metastatic deposits. Multiple well-defined, rounded pulmonary nodules of variable sizes were seen in left lung field, predominantly in the subpleural regions. These nodules showed irregular enhancement and were suspicious for pulmonary metastatic deposits.

Prior excisional biopsy was not done and patient underwent wide local excision of the lesion, and the specimen was submitted for histopathological examination.

Based on the primary tumour thickness and ulceration, the lesion was clinically staged as cT4b. Radiological evaluation demonstrated lymph node enlargement along with suspicious for distant metastases involving the lung, and vertebral body; therefore, the disease was clinically considered metastatic (cM1). As histopathological confirmation of the radiologically suspected metastatic lesions was not available, the M (metastasis) category was assigned clinically not pathologically.

Gross examination: Specimen consists of skin covered soft-tissue mass measuring 9.6×8.2×2.4 cm [Table/Fig-1]. One brownish to blackish nodular growth is seen measuring 2.3×1.7×1.3 cm [Table/Fig-2]. The growth is 1.2 cm away from superior margin, 2.5 cm away from inferior margin, 4.1 cm away from lateral margin and 3.4 cm away from medial margin.

Microscopic examination: Sections showed ulcerated epidermis overlying a highly cellular malignant neoplasm composed of

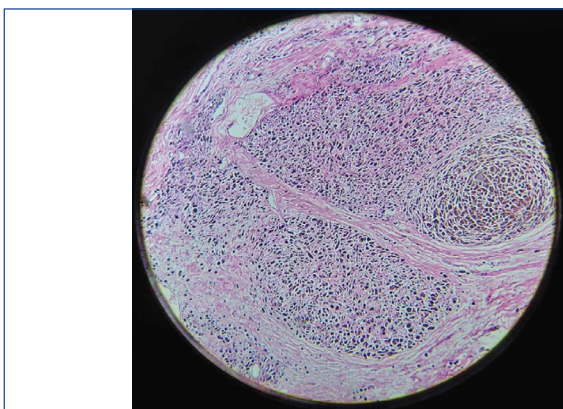


[Table/Fig-1]: Gross image showing wide local excision specimen of nodular, pigmented and ulcerated growth of Nodular Malignant Melanoma (NMM).

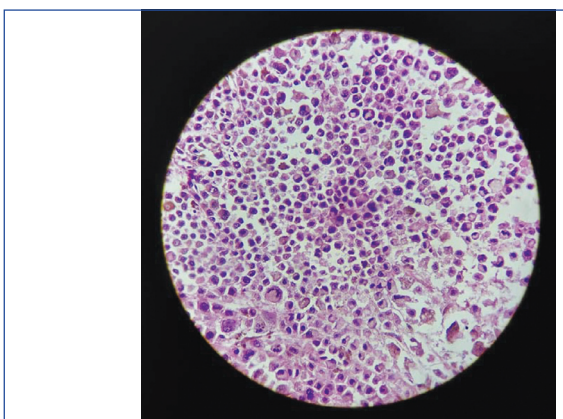


[Table/Fig-2]: Gross image of cut section of Nodular Malignant Melanoma (NMM) growth involving subcutaneous tissue.

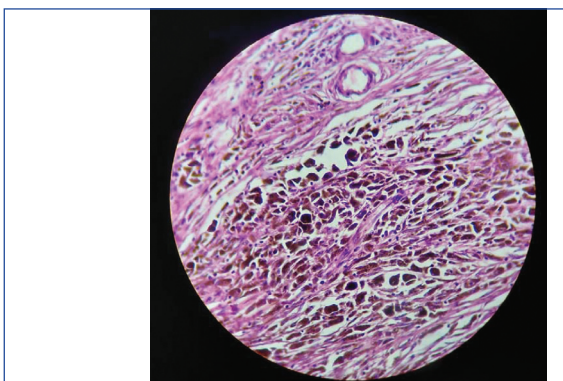
sheets and nests of atypical melanocytic cells infiltrating the dermis. Histopathological examination Haematoxylin and Eosin (H&E) showed tumour cells were predominantly epithelioid with focal spindle cell morphology. Cells exhibited moderate cytoplasm containing melanin pigment, pleomorphic hyperchromatic nuclei and prominent nucleoli [Table/Fig-3-5].



[Table/Fig-3]: Microscopic examination showing malignant melanoma cells arranged in closely packed nest and nodule separated by fibrous septa (H&E, 10x).



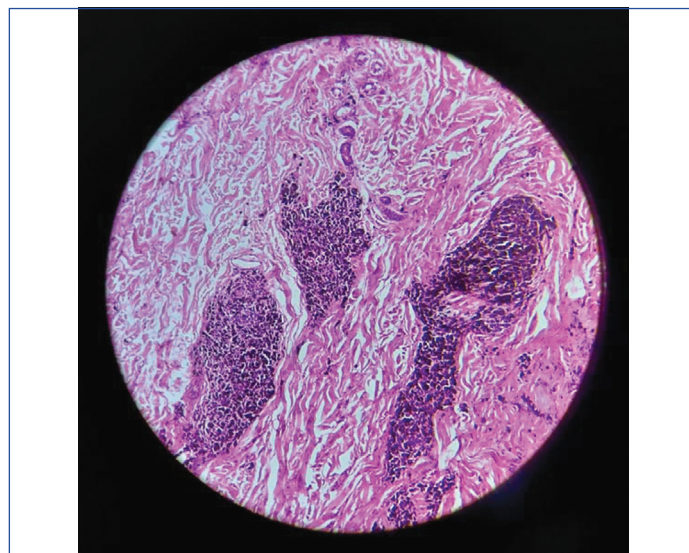
[Table/Fig-4]: Microscopic examination showing malignant melanocytes cells epithelioid morphology with pleomorphic and hyperchromatic nuclei (H&E, 40x).



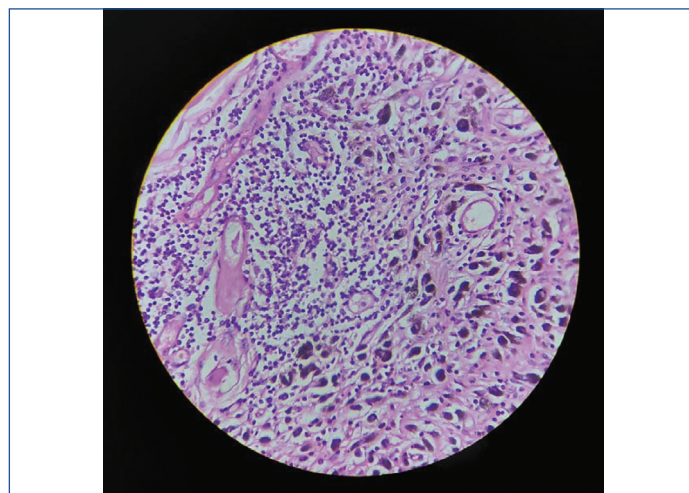
[Table/Fig-5]: Microscopic examination showing atypical melanocytes with intracytoplasmic melanin pigment (H&E, 10x).

Numerous atypical mitotic figures were identified. Intracytoplasmic and extracellular melanin pigment deposition was evident. Tumour infiltration extended into the reticular dermis with evidence of vertical growth. The surgical margins were free of tumour. Histological diagnosis was malignant melanoma - nodular type. Differential diagnosis mimicking similar histological features considered for this case were poorly differentiated Squamous Cell Carcinoma (SCC), pigmented Basal Cell Carcinoma (BCC) and cellular blue nevus. Lymph nodes were not submitted.

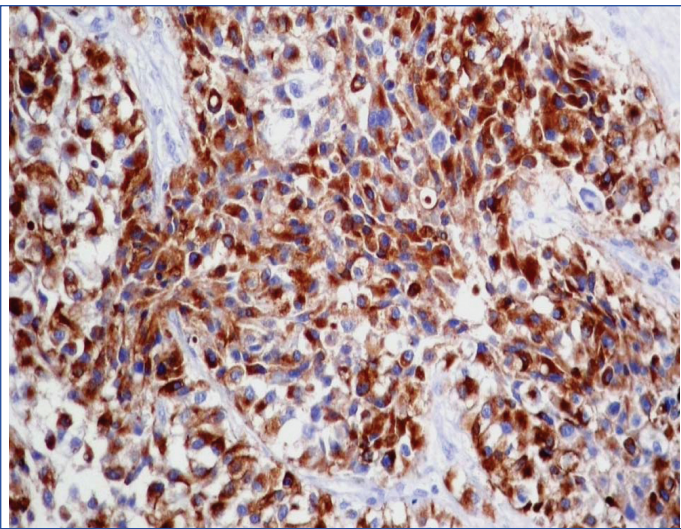
Histological parameters: The histopathological examination revealed nodular melanoma with microsatellitosis [Table/Fig-6]. The Breslow thickness was 13 mm, with lymphovascular invasion present and perineural invasion absent. Focal tumour regression was identified, involving $\leq 75\%$ of the tumour. The tumour showed Clark level V invasion, extending into the subcutaneous tissue. The mitotic rate was 18 mitoses/mm². Ulceration was present. Neurotropism was not identified. Tumour-infiltrating Lymphocytes (TILs) were present and non brisk [Table/Fig-7]. The tumour was located 0.7 cm from the deep resection margin. The radial growth phase measured 4mm. Immunohistochemical evaluation was performed to confirm the diagnosis. The tumour cells showed strong positivity for Melan-A and Human Melanoma Black-45 (HMB-45) [Table/Fig-8], while Pan-cytokeratin (PanCK) was negative in the tumour cells. Ki-67, a marker of cellular proliferation, showed a high proliferative index of approximately 65-70%. Molecular testing for BRAF mutation was not performed. Based on the histopathological findings, the pathological primary tumour category was pT4b.



[Table/Fig-6]: Microscopic examination showing microsatellitosis in which discrete dermal nests of malignant melanoma cells separated by intervening uninvolved dermal tissue (H&E, 10x).



[Table/Fig-7]: Microscopic examination showing lymphocytes infiltration below the nest of malignant melanoma cells (H&E, 40x).



[Table/Fig-8]: HMB-45 immunohistochemistry showing strong cytoplasmic positivity within the malignant melanocytic cells (IHC, $\times 40$).

Biopsy specimens from the radiologically suspected metastatic sites, including the lung, lymph nodes, and vertebral body, were not available for histopathological examination. Therefore, in the absence of histological confirmation of distant metastasis, the pathological primary tumour category was assigned as pT4b based on the primary tumour characteristics. Following surgical excision, the patient was referred to a tertiary oncology centre for BRAF V600 mutation testing and further oncological evaluation. In view of the high-risk pathological features, including the aggressive nodular subtype and adverse histopathological characteristics, adjuvant anti-PD-1 immunotherapy was considered as a potential therapeutic option.

DISCUSSION

The NMM is the most aggressive subtype of cutaneous melanoma because of its rapid vertical growth, deep tissue invasion, and high metastatic potential, resulting in poorer outcomes than other melanoma subtypes [1]. NMM can arise at various cutaneous sites, with a recognised predilection for certain head-and-neck locations. In the present case, the tumour arose in the left supraclavicular region, representing an uncommon site within the broader head-and-neck distribution [2]. Although the Asymmetry, Border irregularity, Colour variation, Diameter and Evolving (ABCDE) criteria are widely used for melanoma detection, presented case of NMM failed to meet these features because the lesion was firm in consistency, raised above the surrounding skin, and rapidly growing. Instead, the Elevated, Firm, Growing (EFG) rule is more useful for its clinical recognition [3]. In this case, patient had an ulcer over nodular lesion. Ulceration is an independent adverse prognostic factor in melanoma and is associated with increased risk of recurrence, metastasis, and reduced survival [4].

The NMM characteristically lacks a prolonged radial growth phase, leading to increased Breslow thickness at presentation [5]. In the present case, the tumour demonstrated a Breslow thickness of 13 mm, indicating marked vertical tumour invasion. Breslow thickness is one of the most important histopathological prognostic parameters in cutaneous melanoma and forms a major component of the American Joint Committee on Cancer (AJCC) T category. Breslow thickness of tumour with >4.0 mm is classified as T4, with subdivision into T4a or T4b depending on the presence or absence of ulceration [6], which is strongly associated with lymph node involvement, distant metastasis, recurrence, and poor survival [7].

Previously published case of aggressive NMM reported by Myers DJ demonstrated a Breslow thickness of 10.1 mm, Clark level IV and pT4b disease. Importantly, radiological evaluation demonstrated metastatic involvement of the bilateral axillary lymph nodes, lung and bone. This case closely resembled the present case in terms

of the combination of a markedly increased Breslow thickness and evidence of distant disease on imaging [8]. The presence of microsatellitosis further indicates intralymphatic spread and is an independent adverse prognostic factor associated with lymph node positivity and reduced melanoma-specific survival [9]. Microsatellitosis had also been reported in previously published case of rapidly progressive acral nodular melanoma of the heel, histopathological examination demonstrated a prominent nodular vertical growth component, lymphovascular invasion and microscopic satellitosis [10]. The aggressive pathological profile observed in the present case is comparable to previously reported case by Kamińska-Winciorek G of giant nodular melanomas, in which marked tumour thickness, ulceration, microsatellitosis and high mitotic activity were associated with an aggressive phenotype [11]. Histopathology also demonstrated TILs. Although brisk TILs generally indicate a favourable host immune response and improved prognosis, their beneficial effect may be outweighed in advanced melanoma by other high-risk features such as marked Breslow thickness, ulceration, microsatellitosis, and metastatic disease [12,13]. Computed tomography revealed regional lymph node enlargement, bony lytic lesion and pulmonary nodules suggesting metastatic deposits, indicate both lymphatic and hematogenous dissemination. Lymph node involvement is one of the strongest predictors of poor prognosis, and its risk increases with greater Breslow thickness, ulceration, and high mitotic activity [14], all of which were present in present case. Bony lytic lesions signifies advanced systemic disease and carries a poor prognosis. Although skeletal involvement is less common than metastases to the lungs, liver, or brain, it occurs in approximately 11-17% of patients with metastatic melanoma and is associated with significantly reduced overall survival [15].

Gullapalli K et al., reported a case of widely metastatic melanoma with osteolytic skeletal lesions accompanied by pulmonary, soft-tissue and mediastinal lymph-node metastases, highlighting the aggressive and multisystem metastatic potential of malignant melanoma [16]. The co-existence of extreme Breslow thickness, ulceration microsatellitosis, and TILs in the present case highlights the highly aggressive nature of NMM and underscores the importance of early recognition, prompt histopathological diagnosis, and comprehensive staging. The principal histopathological differentials of NMM were pigmented BCC, poorly differentiated SCC, and cellular blue nevus. NMM was mimicking pigmented BCC because of abundant melanin; however, the presence of basaloid nests, peripheral palisading, stromal retraction favour BCC. In contrast, this case demonstrated atypical melanocytic proliferation with marked nuclear pleomorphism, prominent nucleoli, mitotic activity and HMB45 positivity excluding pigmented BCC diagnosis. One another differential was poorly differentiated SCC which characteristically show minimal or absent keratinisation and therefore it closely resembled to epithelioid cells of malignant melanoma. Present case did not show any evidence of squamous differentiation, including focal keratinisation or intercellular bridges and showed immunopositivity for HMB45 so diagnosis of poorly differentiated SCC was excluded. Cellular blue nevus was also an important differential in this case. Cellular proliferation of spindle or ovoid melanocytes with abundant melanin and characteristic blue-nevus architecture are its typical histological features [17]. In contrast present case showed marked cytological atypia, increased or atypical mitoses and destructive infiltrative growth and nest like arrangement of atypical cells which favoured diagnosis of NMM.

CONCLUSION(S)

The present case underscores the highly aggressive nature of NMM, demonstrating multiple adverse prognostic features, including high Breslow thickness, ulceration, high mitotic activity, and satellitosis, resulting in pT4b staging according to American Journal of

Cancer Committee (AJCC) 8th edition criteria. The concurrence of these high-risk features highlights the importance of meticulous histopathological evaluation and accurate staging, particularly in clinically atypical presentations, to facilitate timely risk stratification and appropriate management. At the time of manuscript preparation, BRAF mutation status was unavailable; consequently, definitive treatment planning was deferred pending the results of molecular testing.

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