A rare case of disseminated malignant melanoma

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ABSTRACT

Malignant melanomas arise from the various tissues harboring melanocytes including skin, mucocutaneous junctions, conjunctiva, iris, and choroids. They may metastasize to various organs including the skin itself but their presentation, as metastatic cutaneous nodules, is rare. Hereby, a case of metastases of melanoma with unknown primary is being reported, where a young adult male presented with cutaneous nodules of melanoma and metastatic deposits in the lungs and brain.

KEY WORDS: Malignant Melanoma; Melanoma; Cutaneous Metastases

INTRODUCTION

Melanomas are malignant tumors arising from the melanocytes which may arise in the skin or other tissues harboring melanocytes, such as mucocutaneous junctions, mucosa including the conjunctiva, iris, choroids, and substantia nigra.[1] Metastasis to the skin and subcutaneous tissues from a malignant melanoma are not so common. Rarely, there may not be any evidence of primary melanoma and the cutaneous metastasis being the only manifestation of the disease.[2] Various studies in the past have described the patterns of cutaneous metastasis secondary to malignant melanoma including the metastatic nodules, but only a few have reported it as a presenting feature.[2-7] We, hereby report a case of disseminated malignant melanoma in a young adult male with unknown primary presenting with cutaneous metastatic nodules.

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CASE REPORT

A 19-year-old male presented with multiple, firm to hard, asymptomatic, skin colored to light brownish, mobile, nodular lesions, ranging from 1 × 1 to 8 × 6 cm in size over head and neck, trunk, and extremities for the last 7 months (Figure 1). There were progressive dyspnea and significant weight loss, pallor, inguinal, and axillary lymphadenopathy. Routine investigations revealed microcytic hypochromic anemia (Hb- 7.6 g %, mean corpuscular volume-70.4 fl, and red blood cell count-3.36 million/mm^3) and mildly deranged liver function tests (aspartate aminotransferase-86 IU, alanine aminotransferase-98 IU, and alkaline phosphatase-210 IU). Aspiration cytology of the subcutaneous nodules showed marked anisokaryosis, hyperchromatic and stippled nuclei, prominent nucleoli, intranuclear inclusions, and pigment laden melanophages (Figure 2a). Histopathology revealed pleomorphic tumor cells with pleomorphic round to oval eccentric nuclei, prominent eosinophilic nucleoli, multinucleate giant cells with intracytoplasmic melanin pigment, and atypical mitotic figures (Figure 2b). Computed tomography (CT) scan of the thorax showed multiple enhancing parenchymal and pleural-based metastatic nodules in both the lungs with necrotic lymphadenopathy (Figure 3a). CT head revealed

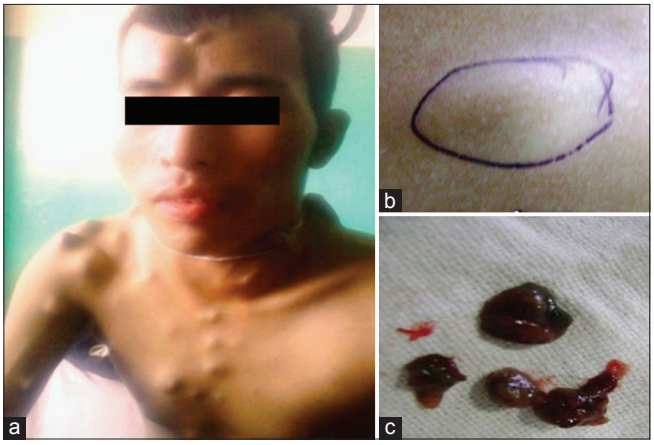

Figure 1: (a) Multiple, well defined, skin colored, firm to hard nodules over face, neck, chest, and girdle area, (b) a firm to hard, non-tender, slightly hyperpigmented nodule over the trunk, (c) excision biopsy specimen of the nodule showing tan brown soft tissue

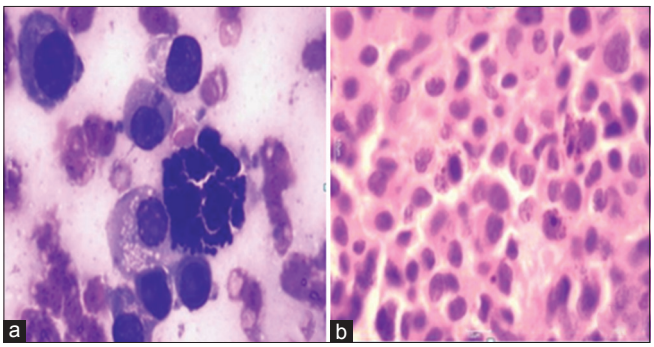

Figure 2: (a) Cytology of the nodules showing anisokaryosis, hyperchromatic and stippled nuclei, prominent nucleoli, intranuclear inclusions, and pigment laden macrophages (H and E; ×100), (b) histopathology showing pleomorphic tumor cells with pleomorphic round to oval nuclei, prominent eosinophillic nucleoli, multinucleate giant cells with intracytoplasmic melanin pigment and atypical mitotic figures (H&E; X100).

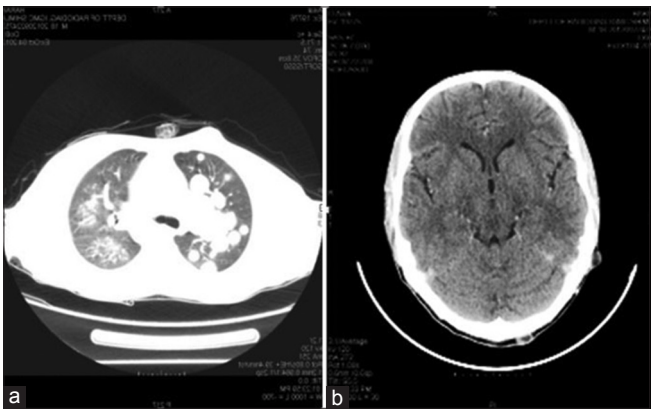

Figure 3: (a) Computed tomography thorax showing multiple pleural and parenchymal based enhancing nodules, (b) computed tomography head showing hyperdense lesion in right temporal region with perilesional edema

intracranial metastasis with soft tissue metastasis of scalp (Figure 3b). The diagnosis of disseminated malignant melanoma was made on the basis of clinicopathological and radiological evidence.

DISCUSSION

Malignant melanoma is a malignant tumor arising from the pigment cells-melanocytes.[8] The pathogenesis of malignant melanoma is unclear. Risk factors can be genetic, environmental (intense, intermittent exposure to sunlight), melanocytic nevi, and personal history of melanoma. The major gene involved in melanoma development resides on chromosome 9p21. This gene is known as CDKN2A (INK4a) encodes two separate protein products, p16 and p14, which are both negative regulators of cell cycle progression, which ultimately cause the development of cancer.[9]

Melanomas spread via lymphatics or by hematogenous dissemination. Metastatic or Stage IV malignant melanoma is a devastating disease and is defined by dissemination of the cutaneous tumor to other organs or non-regional lymph nodes.[7] The skin, subcutaneous tissues, and lymph nodes are the first site of metastatic disease in 59% of patients.[10] Cutaneous metastasis of malignant melanoma can occur in the form of subcutaneous nodules distributed throughout the body, which may be the presenting feature in approximately 10% of the cases.[6] Various studies in the past have mentioned, the patterns of cutaneous metastasis secondary to malignant melanomas. Brownstein and Helwig observed that melanoma was the third most frequent malignancy (males-13% and females-5%) with secondary deposits in the skin.[3] Lookingbill et al. in a large retrospective study found that the cutaneous metastasis was the most frequent sign of extranodal metastatic disease particularly in patients with melanoma.[4] Similar observations were made by Schwartz in 1995 who concluded that melanoma was the third most frequent malignancy to have cutaneous metastasis.[5] Marcoval et al. in their retrospective study, analyzed the clinicopathological features of cutaneous infiltration by cancer and observed that cutaneous metastasis due to melanoma was frequent (nodules being the most common pattern) but was present only in 8% of the patients at the time of initial diagnosis. Nearly half of the patients developed cutaneous metastasis after the initial diagnosis.[6] Recent study by Plaza et al. also observed that there might not be any evidence of primary melanoma in 8.3% of the patients and the cutaneous metastasis may be the only manifestation of the disease. The histologic diagnosis of cutaneous metastatic melanoma can pose difficulties for diagnosis, especially in the face of an unknown primary neoplasm.[2] This case had multiple painless cutaneous nodules over face, trunk, and extremities, as a presenting feature of the disease. Although the cutaneous nodules on histopathology depicted features of melanoma, the primary tumor could not be found. Padmavathy et al. in 2008, reported a similar case with multiple painless nodules that revealed metastatic deposits of melanoma on histopathology

with unknown primary tumor.[7] Overall, in over 4% of patients with metastases, no primary tumor could be found. Hematogenous dissemination can give rise to widespread metastasis as was observed in our patient, who in addition to cutaneous metastatic nodules also had metastasis to the brain and lungs. It carries a grave prognosis with an overall median survival of approximately 7 months. The survival is better in those with nonvisceral disease and with fewer metastatic sites.[10] The most common cause of death from metastatic melanoma is the replacement of pulmonary parenchyma by tumor, and causing respiratory failure.[6]

The search for a primary tumor, in this case was advised, but the patient denied further investigations and treatment, and was lost to follow-up. Treatment for metastatic disease remains unsatisfactory. Many drugs have been used, such as dacarbazine, temozolomide, vinca alkaloids, nitrosoureas, tamoxifen, and immunotherapy, with varying results.[10]

CONCLUSION

The possibility of metastatic melanoma should be kept in mind while evaluating a patient with multiple asymptomatic cutaneous nodules. In a patient suspected with melanoma, thorough medical history, and radiologic investigations should be carried out (especially in Stages III and IV disease). Metastatic nodules signify a poor prognosis. Rarely, cutaneous metastases may be the only manifestation of the disease. In view of the numerous lesions in our patient along with visceral metastasis, surgery was not contemplated and he was lost for follow-up.

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