manifestations after pazopanib therapy, does not allow to exclude its negative influence on the course of sarcoidosis.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship
Nil.

Conflict of interest
There are no conflicts of interest.

Mario Vaccaro, Francesco Borgia, Maria Lentini[1], Michele Gaeta[2], Ilenia Marafioti

Department of Clinical and Experimental Medicine, Dermatology, [1]Human Pathology, [2]Department of Biomedical, Dental Science and Morphological and Functional Images, Radiology Unit, University of Messina, Messina, Italy.

Corresponding author:
Dr. Ilenia Marafioti,
Via C. Valeria, Gazzi. 98125 Messina,
Italy.
ileniamarafioti@gmail.com

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Unilateral nodular malignant melanoma with in-transit metastasis over lower limb masquerading as vascular tumours: A unique presentation

Dear Editor,

A 50-year-old man presented to outpatient department of dermatology, All India Institute of Medical Sciences, Bhubaneswar, with multiple asymptomatic, pigmented, nodular lesions over right lower limb. Initially, there was a single nodular lesion near the right ankle one year ago, which had been excised at a local hospital. He gradually developed multiple new nodules over the same limb in a linear fashion starting from lower part in a span of seven–eight months. The whole limb was swollen and enlarged. He had undergone surgery in the right inguinal region eight months ago. There was no history of any constitutional symptoms, weight loss, loss of appetite or respiratory symptoms. On dermatological examination, multiple dome-shaped, smooth, glossy, pigmented, firm, non-tender, 2–3 mm nodular lesions and 4 cm × 7 cm plaques were found on the right lower limb with underlying skin showing woody-hard induration. The lesions were showing verrucosity, ulceration and crusting on surface [Figures 1a and b].

There was bilateral enlarged inguinal lymphadenopathy with firm-to-hard, discrete nodes of 2–3 cm size. General and systemic examination revealed no abnormality. Routine hematologic and biochemical investigations were within normal limits except for the presence of anaemia (Hb - 7.4 g/dl). His serology for HIV, HBsAg and HCV was normal. Kaposi sarcoma, angiosarcoma and nodular melanoma were considered as differential diagnoses. Other investigations such as chest X-ray, ultrasonography of abdomen and pelvis, computed tomography scan of abdomen and pelvis and magnetic resonance imaging of spine for metastasis were found to be normal. MRI of right leg showed lobulated swellings in cutaneous and subcutaneous planes. On histopathological examination, sections showed a proliferative growth in the upper dermis with plenty of tumour cells, that were polygonal with hyperchromatic nuclei, perinuclear halo, prominent nucleoli and increased mitotic activity [Figures 2a and 2b]. Melanin

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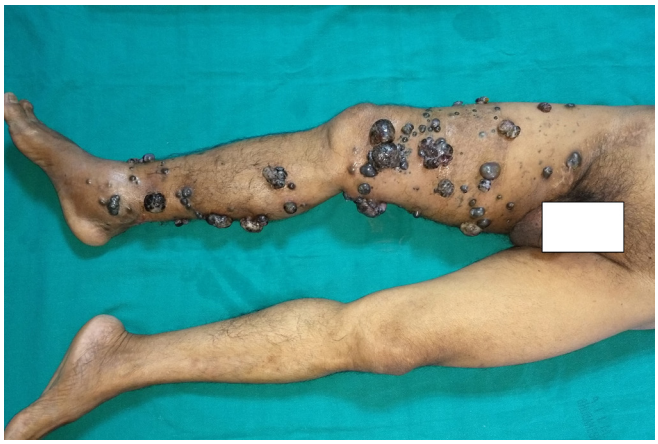

Figure 1a: Unilateral limb involvement of tumours

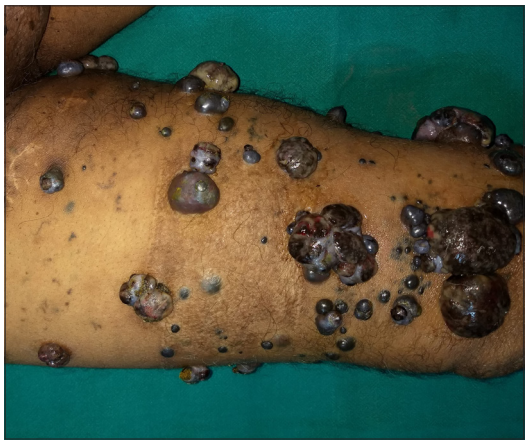

Figure 1b: Close up view showing Pigmented nodules of varying sizes with superficial ulceration

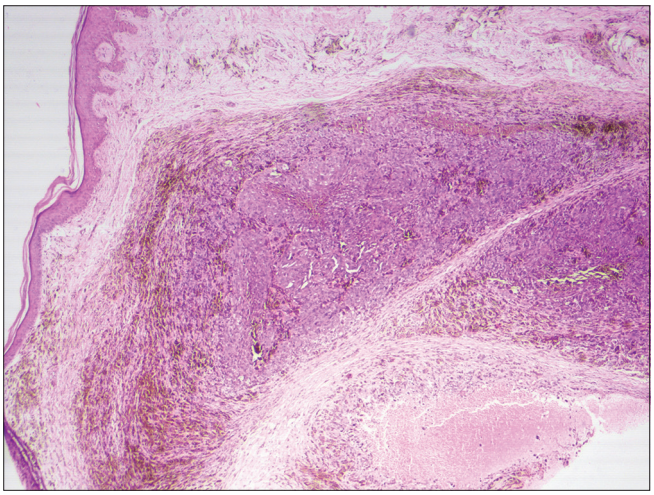

Figure 2a: Scanner view showing nodular collection of tumour cells in dermis (H &E, ×20)

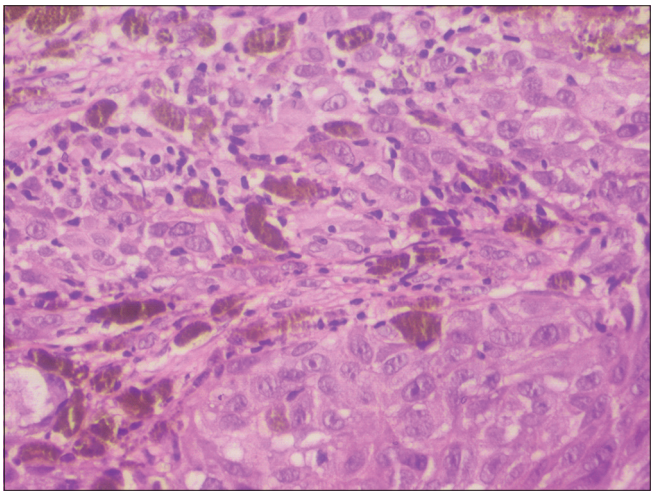

Figure 2b: High power view showing pleomorphic tumour cells with hyperchromatic nuclei, perinuclear halo, prominent nucleoli, intracytoplasmic yellowish-brown pigment and increased mitotic figures (H &E, ×400)

pigment was frequently seen and the tumour cells stained positive for HMB 45 and Melan-A [Figures 2c and 2d], leading to the final diagnosis of malignant melanoma. Fine needle aspiration cytology from the inguinal lymph nodes showed pleomorphic pigmented cells. The tumour was staged as T4N2MO (Stage IIIC) depending on the size and nodal involvement. He was started with temozolomide 150 mg per square metre once a day for five days with 23 days off in a cycle. There was reduction in tumour size after two cycles of treatment [Figure 3]. He is now on follow-up with oncology department and on chemotherapy.

Malignant melanomas were, divided initially by Clark *et al*. using clinical and pathological features into three subsets, superficial spreading, nodular melanoma and lentigo maligna. Later, Reed *et al*. added acral lentiginous melanoma subtype.[1,2] Melanomas are rare in India. Now, its incidence is increasing among Indians and is associated with the majority of skin cancer-related deaths.[3] Nodular melanoma and melanoma d'emblee are rare types of primary cutaneous malignant melanoma that are invasive and lack intraepidermal component.[4] Clinically, it presents as pigmented papules, nodules, nodules with ulceration and rapid increase in size of the tumour. Ulceration occurs fairly early. Our case has similar nodular and noduloulcerative plaques with unique feature of involvement of unilateral limb. This can be possibly due to lymphatic spread of melanoma. There are rare reports of disseminated malignant melanoma presenting as multiple asymptomatic, nodular lesions on the trunk, extremities and the face.[5] Rarely, a sporotrichoid pattern of distribution of malignant melanoma lesions has been reported in literature.[6] We could find very few reports which had depicted a unilateral distribution of malignant melanoma.[7,8] The National Institute of Health consensus have emphasized the use of the asymmetry, border irregularity, colour variegation,

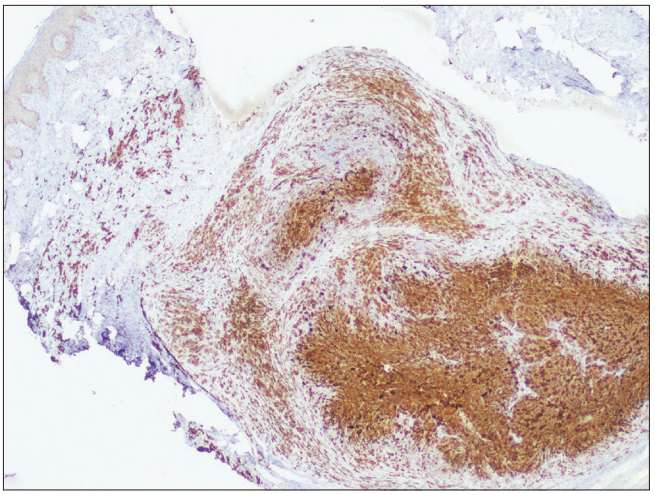

Figure 2c: Immunohistochemistry from nodular skin lesion showing HMB-45 positivity of tumour cells (×20)

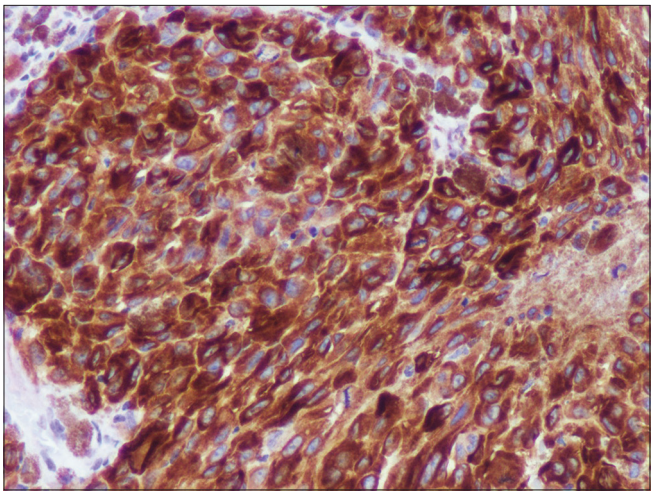

Figure 2d: Immunohistochemistry positive for Melan-A (×40)

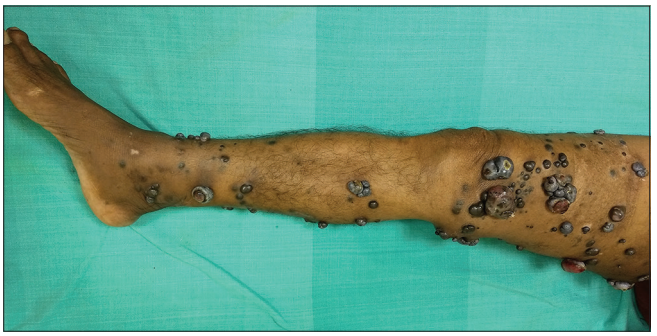

Figure 3: Response two months after starting chemotherapy

diameter >6 mm checklist for the detection of melanocytic lesions. The histological diagnosis of melanoma includes cytological atypia, nuclear pleomorphism, hyperchromatic nuclei, nucleolar variability, presence of mitoses and deposition of melanin. Clinically, our case resembled Kaposi sarcoma, haemangioendothelioma and vascular tumours such as angiosarcoma.[9] Absence of multifocal involvement, upper trunk, head and neck and mucosa involvement and endothelial proliferation in histopathology excludes Kaposi sarcoma. Similarly, angiosarcoma and haemangioendothelioma present as dusky blue or red nodules and grow rapidly, appear in nearby area with ulceration on surface with vascular channels infiltrating the normal structures in a disorganized fashion along with the characteristic 'dissection of collagen' in histopathology. Our patient did not show this type of histopathology although. The bluish and violaceous-red lesions on our patient's leg closely resembled the lesions of vascular tumours. We could find only a few reports of cutaneous melanoma metastases resembling Kaposi sarcoma in the literature.[10] Our case resembled vascular tumours like Kaposi sarcoma and hemangioendothelioma, but proved to be malignant melanoma on histopathology and immunohistochemistry. There was no evidence of distant metastasis clinically or on investigation. The patient was referred to oncology and was started on temozolomide and responded to chemotherapy. We report this case for its rarity and to emphasize for consideration of melanoma as a differential diagnosis of unilateral pigmented or vascular-appearing skin conditions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Kananbala Sahu, Chandra Sekhar Sirka[1], Madhusmita Sethy[2], Jeebanjyoti Mishra[1]

Department of Dermatology, Sri Jagannath Medical College and Hospital, Puri, [1]Departments of Dermatology and [2]Pathology, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

Corresponding author:
Dr. Chandra Sekhar Sirka,
Department of Dermatology, All India Institute of Medical Sciences,
Bhubaneswar, Odisha, India.
csirka2006@gmail.com

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Oral ulcers and cutaneous rash as manifestations of differentiation syndrome in acute promyelocytic leukaemia

Dear Editor,

Differentiation syndrome is a well-known complication of all-trans retinoic acid (ATRA), seen in up to 27% of acute promyelocytic leukaemia (APL) patients treated with the molecule.[1] It is also reported to occur with arsenic trioxide (ATO), which is co-prescribed with all-trans retinoic acid in acute promyelocytic leukaemia patients.[2] It usually manifests after 5–20 days of starting treatment and the presence of three of the following criteria should rise the suspicion of differentiation syndrome; unexplained fever, weight gain (more than 5 kgs), pleuro–pericardial effusion, pulmonary infiltrates, hypotension, respiratory distress and renal failure.[1] Diagnosis is primarily based on clinical presentation, after ruling out infections. Dermatological manifestations of differentiation syndrome are less known and rarely described in the literature. Herein, we report cutaneous manifestations in a case of differentiation syndrome and review the existing literature on all-trans retinoic acid-induced mucocutaneous lesions.

A 73-year-old male patient presented with progressive breathlessness, recurrent fever and ecchymoses over bilateral upper and lower limbs of 14 days' duration. Investigation revealed pancytopenia (haemoglobin; 7.3 g/dL; total leucocyte count; 3900/mm^3 and platelet count 13000/mm^3). Serum lactate dehydrogenase was 3045 IU/L, prothrombin time (PT) was 17 seconds (normal 12–15), and activated partial thromboplastin time (APTT) was 32 seconds (normal 36–35). Serum electrolytes and chest radiograph were within normal limits. Bone marrow examination showed >95% promyelocytes and fluorescence *in situ* hybridization for t (15:17) and polymerase chain reaction (PCR) for promyelocytic leukaemia gene–retinoic acid receptor-α (PML-RARA) was positive. Diagnosis of intermediate risk acute promyelocytic leukaemia was made[3] and the patient was treated with oral all-trans retinoic acid (40 mg twice daily) and intravenous arsenic trioxide (10 mg once a day) with improvement in breathlessness, fever and ecchymoses. After three weeks, patient presented with recurrence of fever and breathlessness, painful oral ulcers and swelling and redness of both upper and lower limbs. Examination revealed multiple round to oval coalescing polycyclic superficial ulcers of size 3–4 mm with yellowish base and surrounding erythematous halo over the hard palate [Figure 1]. Patient also had bilateral pitting pedal oedema extending to lower one-third of the legs with overlying diffuse erythema and scaling including soles [Figure 2]. Patient was admitted for evaluation and all-trans retinoic acid and arsenic trioxide were withheld. At admission, blood pressure was 150/88 mm Hg, pulse rate was 90 beats per minute, respiratory rate was

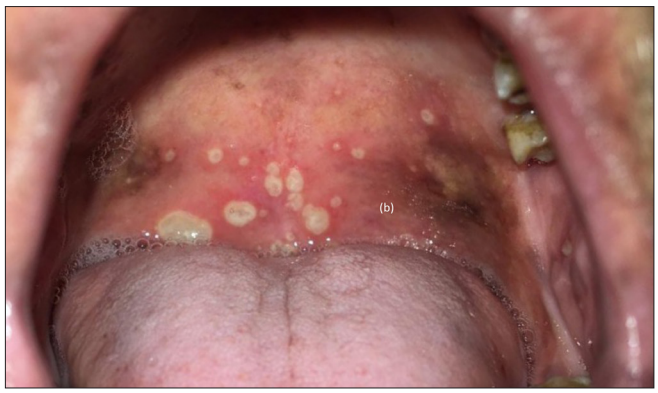

Figure 1: Multiple oral ulcers with yellowish base and surrounding erythematous halo over the hard palate

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