

REFERENCES

1. Yu KK, Crew AB, Messingham KA *et al.* Omalizumab therapy for bullous pemphigoid. *J. Am. Acad. Dermatol.* 2014; **71**: 468–74.
2. Teraki Y, Hotta T, Shiohara T. Skin-homing interleukin-4 and -15-producing cells contribute to bullous pemphigoid: remission of disease is associated with increased frequency of interleukin-10-producing cells. *J. Invest. Dermatol.* 2001; **117**: 1097–102.
3. Shirley M. Dupilumab: first global approval. *Drugs* 2017; **77**: 1115–21.
4. Abdat R, Waldman RA, de Bedout V *et al.* Dupilumab as a novel therapy for bullous pemphigoid: a multicenter case series. *J. Am. Acad. Dermatol.* 2020; **85**: 46–52.
5. Kaye A, Gordon SC, Deverapalli SC *et al.* Dupilumab for the treatment of recalcitrant bullous pemphigoid. *JAMA Dermatol.* 2018; **154**: 1225–6.

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Case Letter

Dear Editor,

*Multicentric reticulohistiocytosis revealing breast cancer:
Report of a case with dermoscopic, radiological and
therapeutic aspects*

Multicentric reticulohistiocytosis (MRH) is a rare non-Langerhans cell histiocytosis of unknown aetiology, and approximately 300 cases are reported in English Literature. Underlying malignancies have been associated with up to 25% of cases; thus, it can be considered a paraneoplastic syndrome.¹ We present here a case of a 48-year-old woman affected with MRH, which was the first sign of breast cancer, focussing on dermoscopic and radiological characterisation of this case. Treatment of MRH is often challenging, but in our patient, a complete regression was achieved after tumour excision without any specific therapy.

A 48-year-old woman presented to our Department for a 10-month history of multiple reddish orange-yellow papules and nodules located on her hands, arms and head (Figure 1a). Dermoscopic examination of the lesions showed yellow surface papules with chrysalis structures, white structureless areas and linear teleangectasias (Figure 1b). The patient also had an 8-month history of symmetrical inflammatory polyarthropathy involving the wrists, elbows, shoulders, knees, ankles and the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of both hands. There was NSAIDs hypersensitivity in her medical

history. A skin biopsy was performed, and histopathological examination showed the presence of histiocytic multinucleated giant cells with ground-glass eosinophilic cytoplasm in the dermis (Figure 1c). A CD68 stain was diffusely positive, and the cells were negative for S100, CD1a and factor XIIIa. A diagnosis of MRH was made.

Since MRH may be a paraneoplastic phenomenon, a 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) was performed to detect possible occult malignancies (Figure 2). 18FDG PET/CT showed an abnormal uptake of FDG in DIP, PIP, wrists, shoulders, knees and ankles. We considered these FDG uptakes as being secondary synovitis of these joints. Foci with increased FDG uptake were observed outside the DIP and PIP joints, corresponding the cutaneous papules and nodules. An elevated FDG uptake was also observed in right axillary lymph nodes, we considered this as a sign of possible internal malignancy, and we referred the patient to General Surgery Department for more investigations.

A lymph-node biopsy and radiological investigations were performed, which detected a ductal carcinoma of the breast. According to Oncologists and General Surgeons, the patient was transferred to Oncology Department. We decided to treat MRH with alendronate 10mg DIE, since immunosuppressant and immunomodulator drugs were contraindicated, but the patient developed a drug eruption after 10 days of treatment, so we decided to stop the treatment and opted for a 'wait-and-see' approach.

The patient underwent mastectomy and axillary lymphadenectomy, followed by radiotherapy and tamoxifen therapy. We followed up the patient weekly and, surprisingly, the cutaneous lesion and the arthropathy improved from the third week after surgery and a complete regression was achieved in 3 months. To date, after 2 years of follow-up, no relapse of MRH and breast cancer have been identified.

Multicentric reticulohistiocytosis (MRH) is a rare cell histiocytosis of unknown aetiology. The disease affects predominantly skin and joints, but visceral involvement is possible.¹

Skin involvement is characterised by multiple flesh-coloured to reddish-brown cutaneous papules and nodules, which mainly involve hands, face and arms.¹ Dermoscopic examination could be useful in diagnosis: the detection of yellow/orange patches is highly suggestive of histiocytic infiltrate in dermis. Similar dermoscopic features have been described in granulomatous skin diseases, sarcoidosis and other histiocytic disorders,² also characterised by granulomatous/histiocytic inflammatory infiltrate, which must be included in differential diagnosis.

Around nail folds can be found small papules with a characteristic coral-bead appearance, and this feature is observed in about 30% of patients and represents a typical clinical sign of MRH.³

The diagnosis of MRH is performed on the basis of the histopathologic findings of cutaneous or synovial tissue specimens. The typical infiltrate is composed of histiocytes and multinucleated giant cells containing eosinophilic cytoplasm with a ground-glass appearance.⁴

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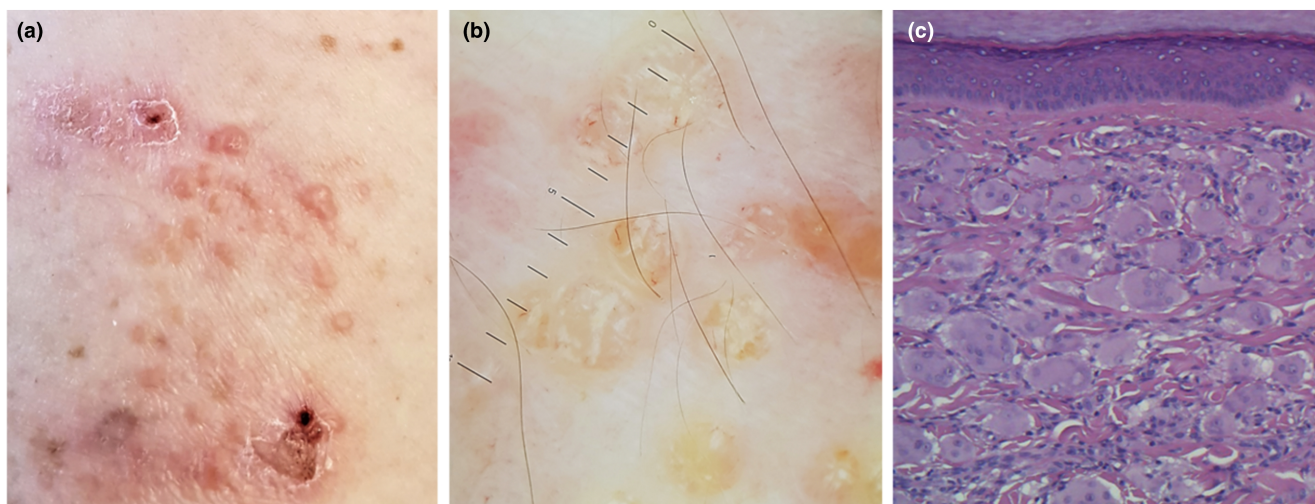


Figure 1 Multiple reddish orange-yellow papules and scratching injuries of left forearm (a); dermoscopic examination shows yellow surface papules with chrysalis structures, white structureless areas and linear telangiectasias (b); histopathology of skin biopsy specimen shows giant multinucleated cells in dermis, haematoxylin and eosin original magnification $\times 40$ (c)

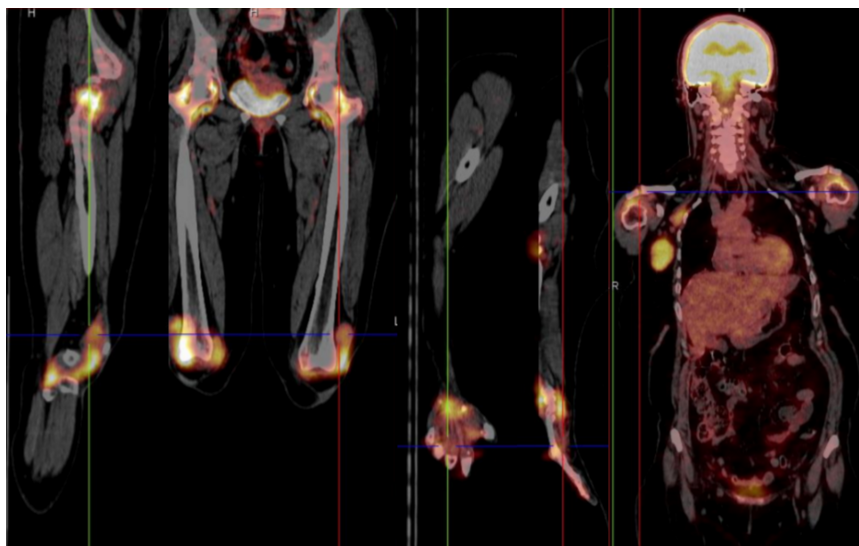


Figure 2 ^{18}F FDG PET/CT image shows an abnormal uptake of FDG in DIP, PIP, wrists, shoulders, knees, right axillary lymph nodes and cutaneous lesions

Radiological investigations should be performed in all patients with MRH to detect possible occult neoplasms. FDG-PET/TC has high overall sensitivity and specificity for detecting cancer⁵ and has an important role in evaluation of inflammatory and granulomatous diseases since FDG is easily taken up by inflammatory cells⁶; thus, it is useful in evaluating the extent of the disease and assessing the possible association of neoplasms.

Treatment of MRH is challenging, and it generally consisted of immunosuppressant and immunomodulators, often contraindicated in patient with a malignant neoplasm. Bisphosphonates have proved effective on both skin and joint involvement, and they can be used as monotherapy or as combination therapy.⁴ In our case, a complete regression of MRH has been obtained after tumour

excision, without any specific therapy, and this suggests that a 'wait-and-see' approach can be considered in patient with paraneoplastic MRH.

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REFERENCES

1. Sanchez-Alvarez C, Sandhu AS, Crowson CS *et al.* Multicentric reticulohistiocytosis: the Mayo Clinic experience (1980–2017).

Rheumatology (Oxford) 2020 (Aug 1); 59: 1898–905. <https://doi.org/10.1093/rheumatology/kez555>.

2. Bombonato C, Argenziano G, Lallas A *et al*. Orange color: a dermoscopic clue for the diagnosis of granulomatous skin diseases. *J Am Acad Dermatol*. 2015 (Jan); 72(1 Suppl): S60–3. <https://doi.org/10.1016/j.jaad.2014.07.059>.
5. Sobjanek M, Sławińska M, Romaszkiwicz A *et al*. Dermoscopic features of periungual papules in multicentric reticulohistiocytosis. *J Eur Acad Dermatol Venereol*. 2017 (Oct); 31: e442–3. <https://doi.org/10.1111/jdv.14260>.
4. Trotta F, Castellino G, Lo MA. Multicentric reticulohistiocytosis. *Best Pract Res Clin Rheumatol*. 2004 (Oct); 18: 759–72. <https://doi.org/10.1016/j.berh.2004.06.002>.
5. Almuhaideb A, Papataniasiou N, Bomanji J. 18F-FDG PET/CT imaging in oncology. *Ann Saudi Med*. 2011 (Jan-Feb); 31:5–15. <https://doi.org/10.4103/0256-4947.75771>.
6. Asano T, Suzutani K, Watanabe A *et al*. The utility of FDG-PET/CT imaging in the evaluation of multicentric reticulohistiocytosis: A case report. *Medicine (Baltimore)*. 2018 (Aug); 97: e11449. <https://doi.org/10.1097/MD.00000000000011449>.

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Case Letter

Diffuse dermal angiomatosis as the first manifestation of myelodysplastic syndrome

INTRODUCTION

Dermal infiltration by non-blastic immature myeloid cells, known as myelodysplasia cutis (MC), is rare, and it can be the first manifestation of a myelodysplastic syndrome (MDS).^{1,2} Clinical appearances of MC range from erythematous plaques to annular or ulcerated lesions, often associated with fever and/or arthralgia.²

CASE REPORT

An 80-year-old man presented with a three-week history of enlarging lesions growing proximally over the upper limbs, which was accompanied by asthenia, anorexia and weight loss for the last two months. Physical examination revealed purpuric plaques extending from wrists to elbows (Figure 1). Laboratory investigations revealed pancytopenia, and imaging studies were normal. Two punch biopsies were taken one week apart.

Histopathology of the first biopsy showed a striking proliferation of dilated capillary vessels along the upper dermis (Figure 2a). The immunohistochemistry demonstrated co-expression of CD31, ERG, D2-40 and a Ki67 higher than



Figure 1 Coalescent symmetric purpuric plaques extending from the wrist of the left and the dorsal surface of the right hands to both elbows, with sharp demarcation. Oedema of the right hand was also noticeable.

50%, while HHV8 was negative. The second biopsy (Figure 2b) demonstrated a slight reduction in the number of blood vessels with a marked decrease in the proliferative index of endothelial cells and a noticeable infiltrate of immature myeloid cells (myeloperoxidase, CD163, CD4, CD15, CD3 and ERG positive). The final diagnosis was MC. Next-generation sequencing performed in the skin biopsy using the Oncomine Myeloid Research Assay failed to detect any mutation, probably because of the suboptimal DNA quality.

Bone marrow study was subsequently performed. The patient was diagnosed with myelodysplastic syndrome with excess blasts-1. Due to cytopenia worsening, 5-azacitidine was given. The cutaneous lesions almost disappeared. However, the patient died 18 months after the diagnosis due to haemorrhagic complications.

DISCUSSION

This case illustrates a new form of MC presentation characterised by a rapid growth of angiomatous lesions resembling clinical Kaposi sarcoma. Histopathology showed a striking vascular proliferation with atypical features (Ki67>50%) and inconspicuous myeloid elements. The sparse medium-sized interstitial ERG-positive myeloid cells in the first biopsy added complexity to the diagnosis. While ERG is a well-known marker of endothelial cells, it can be occasionally expressed in malignant myeloid proliferations.³ Remarkably, the density of the myeloid cellularity clearly increased in the second biopsy, enabling the MC diagnosis.

The few previous reports of malignancy-related DDA were categorised as reactive proliferations associated with neuroendocrine tumours and melanoma.⁴ In the present case, pro-angiogenic activity mediated by tumour-derived soluble factors may account for the vascular proliferation that appeared at a very early stage of the MC. It can be

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