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Necrobiotic xanthogranuloma and polymyositis in a patient with squamous cell lung cancer: a new paraneoplastic entity?

A 64-year-old man presented with a three-month history of skin lesions, muscle weakness and dysphagia. He reported unintentional weight loss of 18 kg over the last year. His past medical history included Type 2 diabetes, arterial hypertension, and chronic obstructive pulmonary disease.
Physical examination revealed asymptomatic, sharply demarcated, erythematous and yellowish non-scaly plaques, mainly on the shoulders, the chest, the proximal extremities and the periorbital region. The lesions varied in size from 5 to 15 cm and were confluent (*figure 1A, B*). Histopathologically, they presented with a diffuse granulomatous infiltrate throughout the entire dermis and upper subcutis, with a vague annular configuration, necrobiosis, and multinucleated giant cells. Immunophenotypically, the infiltrate was composed predominantly of CD163+ M2 macrophages and CD68+ macrophages -some of them with strong intracytoplasmic expression of adipophilin (foamy macrophages). MNDA+ (myeloid cell nuclear differentiation antigen) granulocytes and their precursors were present throughout the infiltrate. Remarkably, the granulomatous infiltrate was admixed and bordered by small clusters of polytypic CD79a+ plasma cells and few CD123+ plasmacytoid dendritic cells (*figure 1C, D*). Thus, we established the diagnosis of necrobiotic xanthogranuloma at an early stage. Due to muscle weakness and elevated creatine kinase levels, biopsy of the deltoid muscle was performed. Histology revealed a perimysial infiltration of predominantly CD3+/CD4+ T-cells, neutrophils, and degenerated muscle fibres, consistent with myositis.
Laboratory work-up revealed elevated levels of leukocytes (28 G/L; normal range: 4-10), ASAT (350 U/L; normal <50), ALAT (460 U/L; normal <50), LDH (646 U/L; normal range: 125-250), and creatine kinase (6,177 U/L; normal <200). The most common tumour markers (CEA, AFP, CA 19-9, PSA, beta-2 microglobulin) were within normal range. There was no sign of monoclonal gammopathy.

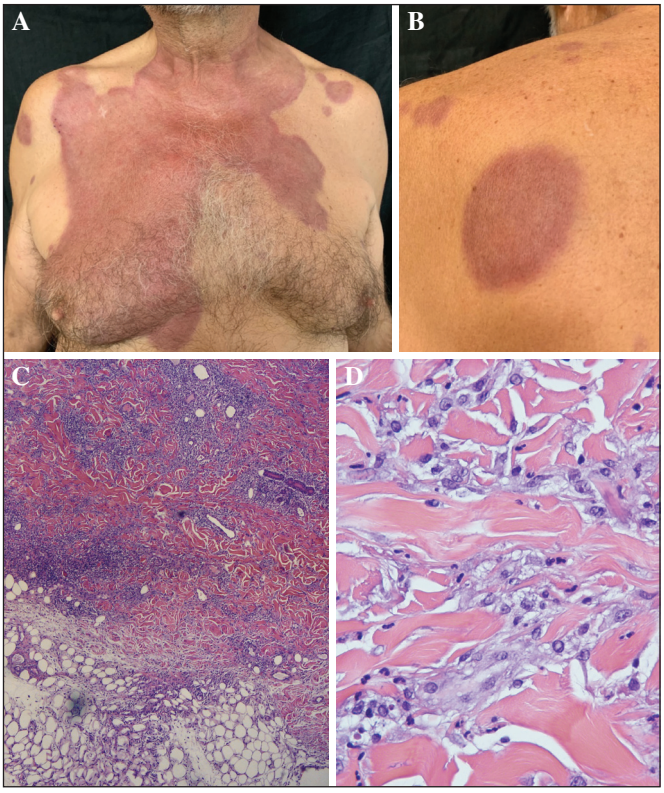

Figure 1. A) Large confluent erythematous plaque on the chest. **B**) Erythematous plaque with a yellowish hue on the dorsum. **C**) Diffuse granulomatous infiltrate, mainly composed of focal aggregated plasma cells, giant cells, foamy histiocytes, and lymphocytes (hematoxylin-eosin). **D**) Collagen fibres with foamy histiocytes in the interstitial areas (haematoxylin-eosin; higher magnification).

Antinuclear antibodies and autoantibodies to extractable nuclear antigens (including anti-Jo-1, anti-Mi-2 and anti-TIF1-gamma) were negative. A CT scan of the chest and abdomen showed several enlarged lymph nodes in the right jugular area and a tumour in the left upper lobe. One lymph node was excised for histological examination. It revealed metastatic spread of a poorly-differentiated squamous cell carcinoma of the lung. After treatment with intravenous immunoglobulins and steroids, regression of myositis and the cutaneous lesions was achieved. The inoperable lung cancer was treated with pembrolizumab, paclitaxel, and cisplatin. The patient died two months later of pneumonia.
We report a patient with squamous cell lung cancer, necrobiotic xanthogranuloma, and polymyositis. In approximately 80% of cases, necrobiotic xanthogranuloma is accompanied by monoclonal gammopathy [1]. Necrobiotic xanthogranuloma may also be associated with blood cancers or lymphoproliferative disorders [2, 3]. No cases associated with lung cancer - as in our patient - or other solid tumours have been reported so far. In our patient, monoclonal gammopathy and leukaemia were ruled out based on immuno-electrophoresis and flow cytometric analysis.
Polymyositis is one of many inflammatory myopathies and is accompanied by symmetrical proximal muscle weakness. About 30% of elderly patients with dermatomyositis/polymyositis have an underlying malignancy. Cancer is less frequent in the presence of polymyositis than dermatomyositis [4, 5]. Associated cancers include those of the ovary, lung, breast, gastrointestinal tract, pancreas, nasopharynx, testicles, and non-Hodgkin's lymphoma. An association between polymyositis and lung cancer has been rarely reported [6]. The pathophysiology of polymyositis and malignancy is not well understood. Some patients with paraneoplastic polymyositis develop autoantigens common to cancer and muscle tissue, resulting in muscle damage [7]. Paraneoplastic polymyositis is frequently resistant to treatment because of the underlying malignancy. On the other hand, the treatment of cancer may lead to the regression of myositis.
To the best of our knowledge, this is the first reported case of necrobiotic xanthogranuloma and polymyositis in a patient with lung cancer. The simultaneous occurrence of these two potentially paraneoplastic diseases in the same patient may constitute a new clinical entity. ■

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Evolution of different clinical patterns of cutaneous lesions in a suspected COVID-19 patient

Cutaneous manifestations of Coronavirus disease-19 (COVID-19) were noted in >20% of hospitalized patients in a recent Italian study [1]. Heterogeneous manifestations have been reported. Suchonwanit *et al.* [2] distinguished two groups: viral exanthemas and thrombotic vasculitides. In a recent Spanish multicentre paper [3], five different patterns were identified: acral erythema (pseudochilblain), vesicular eruptions, urticarial lesions, maculopapular eruptions (the most frequent) and livedo/necrosis.
Herein, we report a patient who sequentially developed two cutaneous COVID-related manifestations; a macular exanthema followed by a livedoid vasculitic eruption, characterised by different pathogenetic and histopathological features. As far as we know, no previous cases have been reported with similar features.
A 58-year-old healthy man developed fever and chills on March 23rd and received hydroxychloroquine and minocyclin at home. On April 4th, he developed a macular rash with confluent erythema on the trunk and limbs, without itching (*figure 1A*). Because of the worsening of fever (up to 40°C), he was hospitalised on April 5th, continuing hydrox-

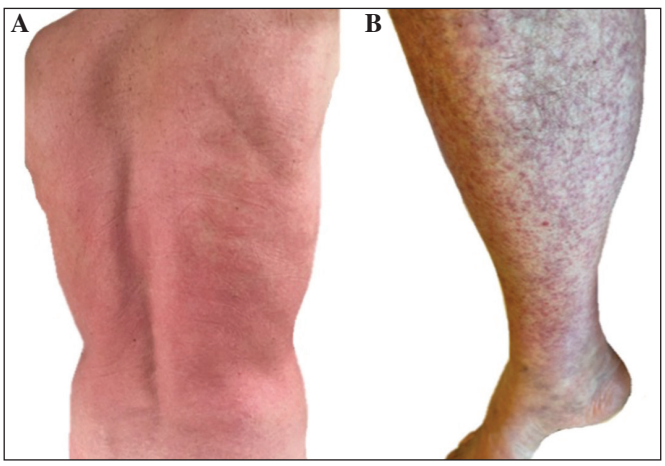

Figure 1. Clinical images of the case: **A**) confluent erythema on the trunk; **B**) livedoid lesions on the lower legs.