Paraneoplastic systemic lupus erythematosus in association with oat cell tumour of the lung

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For AD, patients seen in private dermatology clinics were of similar age and gender distribution and with less hypertension and statin use, compared with hospital-treated patients. Topical pimecrolimus and tacrolimus were more frequently prescribed in private practice, whereas systemic treatment and topical/oral corticosteroids were used considerably more in hospital clinics. Exclusion of the most affluent quintile of the study population yielded similar results for psoriasis or AD (data not shown).

The observed differences in the present study suggest a differential disease burden and treatment patterns among patients seen in hospital outpatient settings compared with private dermatology clinics. More patients seen in hospital clinics have low socio-economic status and a higher comorbidity and disease burden (measured by antipsoriatic therapy use) and may help explain some of the observed disparities in disease associations seen among hospital and general population-based studies for AD and psoriasis.[6–8]

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Editor

Case report: A 63-year-old man presented in the emergency department with general malaise, asthenia, an erythematosquamous rash on face and forearms and severe hyponatremia. The rash appeared after working in his garden on a sunny afternoon without sunscreen protection (Fig. 1a,b,c). Furosemide was stopped, and once daily mometasonfuroate cream was prescribed. Hyponatremia was corrected by IV hypertonic fluids. Five days later, the rash spread to the upper legs, chest and back. Histopathology revealed damage of the basal layer with necrotic keratinocytes and dermal perivascular and adnexal infiltrates (Fig. 2). Direct immunofluorescence (DIF) was negative. The rash resolved during 2 weeks of treatment with systemic methylprednisolone 64 mg, but after stopping oral steroid treatment and despite discontinuation of photosensitizing drugs, a flare appeared within a month. Now clinically and histopathologically, a toxic skin reaction or lupus erythematosus (despite negative DIF) was suspected.

Laboratory workup showed lymphopenia ($0.79.10^3/mm^3$), with normal haemoglobin, platelets and erythrocyte sedimentation rate. Sodium was 114 mmol/L. Antinuclear antibody test was positive (1:640 titre) with speckled pattern and positivity for native ribonucleoprotein (RNP)/Smith (Sm), Sm, RNP-A and RNP-C. Anti-histone antibodies were negative.

One month prior to initial presentation of the rash, a small cell neuro-endocrine lung cancer (oat cell tumour), with tumour masses in the lower right pulmonary lobe and osteoblastic metastases of vertebrae and sacrum (cT1apN2cM1), was detected accidentally during a computer tomography scan for

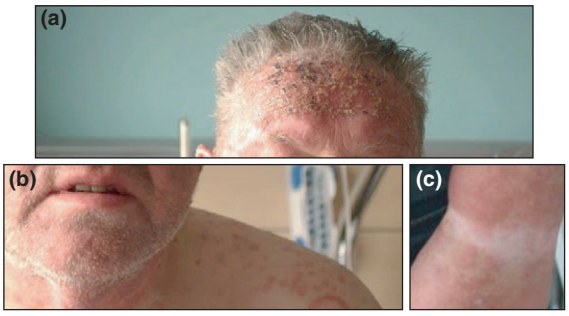

Figure 1 Initial diagnosis: phototoxic reaction to Furosemide. (a, b) erythematosquamous eruption, secondary impetiginized on forehead (a), but also present on neck and shoulders (b) of a 63-year-old man presenting on the emergency department with general malaise, asthenia and severe hyponatraemia. (c) Phototoxic distribution of an erythematomacular eruption on the forearms.

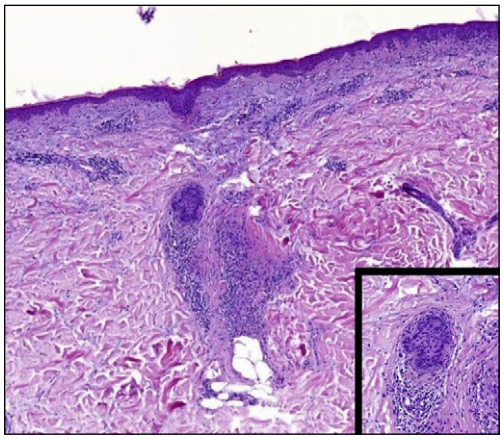

Figure 2 Histopathology. A skin biopsy (haematoxylin and eosin staining, 40× magnification) revealed damage and enlargement of the basal layer of the epidermis with necrotic keratinocytes, plus a dermal perivascular and adnexal infiltrate.

abdominal complaints. Carcinogenic Embryonic Antigen (CEA) was elevated (3.4 μg/L), neuron specific enolase was negative. Therapeutically, thoracoscopic wedge resection and lobectomy were performed. The hyponatremia was considered part of a Syndrome of Inappropriate antidiuretic hormone secretion (SIADH), which frequently accompanies pulmonary neoplasia. Chemotherapy was started with Carboplatin and Etoposide.

Based on the clinical picture (skin lesions progressing after withdrawal of phototoxic drugs), and histopathology, paraneoplastic lupus erythematosus (pLE) was diagnosed (based on the American College of Rheumatology (ACR) and Systemic Lupus International Collaborating Clinics (SLICC) criteria).[1] Oral methylprednisolone was again administered together with topical mometasonfuroate cream. Corticosteroids were gradually tapered and the rash slowly resolved. Six months later, the patient was free of skin lesions but experienced relapses during progression of his oncological disease until he died 1 year after initial skin symptoms.

According to criteria for defining paraneoplastic dermatosis, established by McLean *et al.*,[2] the sequence of events observed in our patient strongly suggests the diagnosis of pLE. In our patient, the rash developed after the accidental finding of a small cell lung carcinoma. In most cases, however, the rash precedes the tumour diagnosis. Furthermore malignancy and dermatosis followed a parallel course in our patient.

Subacute cutaneous and systemic pLE are rarely reported. Since 1984, 33 cases of pLE have been described.[3] An association between pLE and internal malignancy has often been reported for lung carcinoma (mostly epidermoïd non-small cell lung carcinoma)[4] and breast carcinoma, but also for gastrointestinal and head and neck carcinoma. Solitary cases have been reported in association with alveolar soft part sarcoma, meningioma, lymphoma, papillary thyroid carcinoma and acute myeloid leukaemia. Not in all cases, the diagnosis was established using strict diagnostic criteria and nomenclature making it difficult to judge the level of association between the tumour and the autoimmune process. Furthermore, neither the classification of the tumour nor the tumour associated LE-type were discussed consistently in these reports.

This case is one of few cases that associate pLE with pulmonary oat cell tumour and is an instructive example of how paraneoplastic syndromes can be misleading. pLE should be considered in persistent phototoxic reactions in polymedicated patients. Finally, in unclear and recalcitrant exanthemas an underlying hormone or other mediators producing tumour needs to be ruled out.

Y.M contributed to manuscript preparation. Y.M., M.G., V.P. and J.G contributed to patient care. A.DC performed histopathology. M.G., V.P., J.G. and J.R performed manuscript review.

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Treatment of a patient with HIV and metastatic melanoma with consequitive ipilimumab and nivolumab

Editor

Recently new therapeutic agents were developed leading to a paradigm shift in melanoma treatment by the approval of checkpoint inhibitors and targeted therapies. However, in clinical

