Research letter

Comparison of pyoderma gangrenosum and Martorell hypertensive ischaemic leg ulcer in a Swiss cohort

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Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis presenting with painful and sterile skin ulcerations.[1] Its aetiology remains largely unknown, although an autoinflammatory background seems possible. Several comorbidities, as well as triggering factors such as surgery, trauma or pharmacological therapies, have been associated with the development of PG.[2] Different topical and systemic treatments are recommended for PG, most commonly topical steroids or calcineurin inhibitors, as well as systemic steroids, dapsone, infliximab and others. Our group and others have also used canakinumab and ustekinumab.[3,4] PG is a diagnosis of exclusion and is often misdiagnosed at initial manifestation. Martorell hypertensive ischaemic leg ulcer (HYTILU) was previously investigated by our group; we showed that 50% of patients with a referral diagnosis of PG were found to have HYTILU.[5] HYTILU is caused by ischaemic subcutaneous arteriolosclerosis; all patients show arterial hypertension and up to 58% have diabetes mellitus. Typical clinical presentation of HYTILU is a laterodorsal lower leg ulceration with central black necrosis and purple inflamed ulcer borders.[5,6] Clinically, this appearance can be misleading for PG; owing to the risk of septicaemia, immunosuppression could be fatal in HYTILU.[5] In the current study we compared a cohort with PG with a cohort with HYTILU, focusing on clinical data, laboratory findings and comorbidities to develop diagnostic clues for both diseases.

A keyword search for 'pyoderma' and/or 'gangrenosum' was conducted in the files for all patients who were hospitalized between 1 January 2002 and 31 December 2012 at the Department of Dermatology, University Hospital of Zurich (USZ), Cantonal Hospital of Sankt Gallen and at the private practice of W.K. (USZ). In total, 179 patients were identified with an initial suspected differential diagnosis of PG, of whom 38 were diagnosed with PG. We performed a histopathological reassessment of these 38 patients and identified three patients with histopathological signs of HYTILU and one with morphoea, leading to exclusion of these four patients from further analysis. The remaining 34 patients fulfilled the criteria for PG as established by Su et al. and were included in our study.[7] These patients with PG were retrospectively compared with a cohort of 32 patients with HYTILU diagnosed at USZ during the same period. Medical records and laboratory findings were analysed for both cohorts in order to identify features supporting clinical distinction (Table 1). The study was approved by the local ethics committee (KEK ZH 2014-0432). GraphPad Prism® 7.0b 2016 (GraphPad, La Jolla, CA, U.S.A.) and Excel® 14.3.2 2011 (Microsoft, Redmond, WA, U.S.A.) were used for statistical analyses.

Compared with PG, HYTILU was less frequent in women and at older age; more common in smokers; showed higher levels of C-reactive protein (CRP) but lower levels of blood leucocytes and neutrophils; showed lesion localization at the lower leg; and showed more cardiovascular comorbidities such as arterial hypertension, diabetes mellitus, peripheral artery occlusive disease and metabolic syndrome, and more microbial superinfection (Table 1).

Table 1 Comparison of 32 patients with Martorell hypertensive ischaemic leg ulcer (HYTILU) and 34 patients with pyoderma gangrenosum (PG)

	HYTILU ($n = 32$)	PG ($n = 34$)	P-value[a]
Female sex	50	62	NS
Age at manifestation (y)	73.5	61.2	≤ 0.001
BMI (kg m^{-2})	28.3	24.1	≤ 0.05
Smoking	25	21	NS
Alcohol	13	12	NS
Laboratory (mean)			
CRP (mg L^{-1})[b]	31.5	14.5	NS
Leucocytes ($\times 10^9$ cells L^{-1})[c]	9.9	10.5	NS
Neutrophils ($\times 10^9$ cells L^{-1})[d]	7.9	8.4	≤ 0.05
Lesion localization on lower leg	100	67	≤ 0.001
Cardiovascular comorbidities	100	79	≤ 0.01
Arterial hypertension	100	29	≤ 0.001
PAOD	62	6	≤ 0.001
Hypertensive heart disease	41	12	≤ 0.01
Myocardial infarction	25	6	≤ 0.05
Other cardiopathy	12	3	NS
Cerebrovascular infarction	22	3	≤ 0.05
Metabolic syndrome	66	3	≤ 0.001
Diabetes mellitus	53	9	≤ 0.001
Thrombosis	3	9	NS
Renal insufficiency	28	21	NS
Positive microbiological swab	91	44	≤ 0.001

Data are % unless otherwise indicated. NS, not significant; BMI, body mass index; CRP, C-reactive protein; PAOD, peripheral artery occlusive disease. [a]Unpaired t-test with Welch correction. [b]Reference value < 5 mg L^{-1}. [c]Reference value 3.5–9.6 $\times 10^9$ cells L^{-1}. [d]Reference value 1.4–8.0 $\times 10^9$ cells L^{-1}.