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ORIGINAL ARTICLE

Patients with pyoderma gangrenosum – analyses of the German DRG data from 2012

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Abstract

Pyoderma gangrenosum (PG) is a rarely diagnosed non-infectious neutrophil ulcerative dermatosis with only limited knowledge on the underlying auto-inflammatory process. To unravel common cofactors and comorbidities in patients with PG we analysed Diagnosis Related Groups (DRG) cases of all inpatients diagnosed with PG in German hospitals in 2012. We received data of 1227 inpatient cases having PG as primary diagnosis and 985 inpatient cases with PG as secondary diagnosis. The ratio of women to men was 2:1, and the most often registered age was 75–79 years. Common comorbidities were arterial hypertension (50·3%), non-insulin-dependent diabetes mellitus (25·1%) and dysfunction of lipid metabolism (10·8%). In sum, 94·8% of the patients suffered from aspects of metabolic syndrome. Other comorbidities were Crohn's disease (4·5%), ulcerative colitis (4·2%), chronic polyarthritis (5·2%), monoclonal gammopathy or myelodysplastic syndrome (2·5%), leukaemia (1·1%) and lymphoma (0·4%). DRG data do not reflect individual patients, but rather patient cases. We described the worldwide largest PG population and confirmed a wide range of potentially relevant and partly not yet described cofactors and comorbidities such as metabolic syndrome.

Introduction

Pyoderma gangrenosum (PG) is a rarely diagnosed non-infectious neutrophil ulcerative orphan disease with only limited knowledge on the underlying auto-inflammatory process (1,2). In most cases, PG is indirectly diagnosed by exclusion of other diseases according to clinical or histological features. The diagnosis of PG relies on the characteristic clinical appearance including extremely painful ulcers with dark-purple, undermined wound margins developing from primary sterile pustules or nodules (2). There is a controversy on the discussion whether biopsies should be taken for diagnostics, because of the risk of a pathergy phenomenon and the lack of histopathologically specific findings. Nevertheless, histology may still help to exclude other differential diagnoses with clearer histological features such as vasculitis, vasculopathies and cancer (3). In the past decades, the association of PG with inflammatory bowel diseases (IBDs), hepatitis C, seronegative rheumatoid arthritis (RA), spondylitis

Key Messages

- pyoderma gangrenosum is an orphan disease with only limited knowledge on the underlying auto-inflammatory process
- this investigation describes the worldwide largest population and confirms a wide range of potentially relevant comorbidities
- knowledge on concurrent diseases may improve the underlying pathophysiology and identification of persons with elevated risks

and a broad spectrum of lymphoproliferative disorders including monoclonal gammopathy, leukaemia, lymphoma and myelodysplastic syndrome has been described (4–6). However, these observations and the descending current textbook knowledge are only based on small epidemiological evaluations from cohorts of 86 patients (7,8). Up to date, the largest epidemiological study came from the UK analysing the mortality rates of 313 patients with PG compared with control groups comprising the general population and patients with RA or IBD. This report demonstrated that the risk of death was three times increased in PG patients when compared with the general population, 72% higher than for IBD and borderline increase for RA patients. Associations with other diseases could be demonstrated in 110 (33%) patients: in 67 (20·2%) patients with IBD, in 39 (11·8%) patients with RA and in 13 (3·9%) patients with haematological disorders (9). A current multicentre study in Germany comprising 259 patients pointed to additional cofactors and comorbidities such as metabolic syndrome and endocrinological diseases (1).

The awareness of the associated aspects is very important for the future improvement of our pathophysiological understanding of PG as a distinct entity as well as for diagnostic and therapeutic approaches.

Material, methods and patients

Patients

Since its introduction in 2005 in Germany, the Diagnosis Related Groups (DRG) system represents the administrative basis for the financial compensation of general hospital services. The DRG statistics from all German hospitals are registered at the German Federal Statistical Office accounting for more than 99% of all inpatient treatments. German hospitals are legally obliged to submit data on diagnosis, treatment and demographics to the Institut für das Entgeldsystem im Krankenhaus (inEK), which transfers them to the German Federal Statistical Office. This procedure allows a continuous adaption, update and further development of the DRG system (10). For this study, the German Federal Statistical Office provided us with the DRG data of the year 2012. The focus of the study was on cofactors and comorbidities of patient cases with PG as the primary or secondary diagnosis as represented by the International Statistical Classification of Diseases and Related Health Problems (ICD) code L88.

Data

The age-adjusted prevalence and the gender and age distribution of PG patients were provided by the German Federal Statistical Office, which consisted of two separate data sets, one for PG as primary and another for PG as secondary diagnosis. Importantly, these data refer to treatment cases and not to single individual patients.

Statistical analysis

All calculations were performed using Microsoft™, Redmond, USA Excel for Mac 2011.

Table 1 Epidemiological distribution of patient cases with PG as the primary diagnosis in 2012

Age	Total	Male	Female
<1	–	–	–
1–5	–	–	–
5–10	–	–	–
10–15	1	1	–
15–20	10	3	7
20–25	14	5	9
25–30	22	11	11
30–35	23	9	14
35–40	27	10	17
40–45	83	29	54
45–50	68	24	44
50–55	111	41	70
55–60	143	75	68
60–65	111	56	55
65–70	114	56	58
70–75	143	68	75
75–80	192	71	121
80–85	102	19	83
85–90	43	5	38
90–95	20	4	16
>95	–	–	–
Unknown	–	–	–
Total	1227	487 (39·7%)	740 (60·3%)

PG, pyoderma gangrenosum.

Results

Demographics

We analysed the data of 1227 patient cases with PG as the primary diagnosis. In addition, 985 patient cases were documented with PG as the secondary diagnosis. In both groups, females were more often affected (60·3% women versus 39·7% men with PG as primary diagnosis, 60·2% versus 39·8% with PG as secondary diagnosis) (Tables 1 and 2). The most often registered age was 75–79 years in both groups (n = 192 with PG as primary diagnosis; n = 176 with PG as secondary diagnosis) (Tables 1 and 2). Apparently, the mean age of these patients increased over the previous years from 65–69 years (2005–2007) to 70–74 years (2008–2011) and finally to 75–79 years (2012). A similar tendency was seen for the group with PG as the secondary diagnosis; 65–79 years in 2005 and 2006, 75–79 years in 2007–2012, however, switching back to 70–74 years in 2008 and 2010. The demographic overview showed that the registered cases with PG as the primary diagnosis continuously increased from 790 cases in 2005 to 1227 in 2012 (2006: 854; 2007: 914; 2008: 1050; 2009: 1111; 2010: 1084; 2011: 1193).

Comorbidities of patient cases with pyoderma gangrenosum as the primary diagnosis

The most commonly documented comorbidities of the 1227 patient cases with PG as the primary diagnosis were essential arterial hypertension in 50·3%, followed by bacterial infection/colonisation, for example, by *Pseudomonas aeruginosa* in

Table 2 Epidemiological distribution of patient cases with PG as the secondary diagnosis in 2012

Age	Total	Male	Female
<1	1	1	–
1–5	–	–	–
5–10	–	–	–
10–15	5	1	4
15–20	6	5	1
20–25	10	3	7
25–30	22	15	7
30–35	24	8	16
35–40	27	11	16
40–45	35	8	27
45–50	44	17	27
50–55	54	26	28
55–60	93	40	53
60–65	101	49	52
65–70	80	34	46
70–75	136	61	75
75–80	176	69	107
80-85	112	28	84
85-90	41	14	27
90-95	15	1	14
>95	3	1	2
Unknown	–	–	–
Total	985	392 (39·8%)	593 (60·2%)

43·0% or *Streptococci* and *Staphylococci* in 39·7% of all PG cases. Diabetes mellitus type II (non-insulin-dependent diabetes mellitus, NIDDM) occurred in 25·1%, obesity in 8·6% and dysfunctions of the lipid metabolism in 10·8% of the cases. In sum, 94·8% of the PG cases harboured signs of metabolic syndrome, which is also known as (dysmetabolic) syndrome X. Diseases of the cardiovascular system were detected in a total of 45·5%, with atrial fibrillation and atrial flutter in 14·3%, chronic ischaemic heart disease in 11·2%, heart failure in 10·2% and atherosclerosis in 9·8%. Other comorbidities were chronic polyarthritis in 5·2%, IBD such as Crohn's disease in 4·5% and/or ulcerative colitis in 4·2%, hepatitis in 0·4%, lymphoproliferative disorders such as monoclonal gammopathy and myelodysplastic syndrome in 2·5%, leukaemia in 1·1%, lymphoma in 0·4%, endocrinological diseases in 16·7%, chronic renal failure in 14·9% and hypothyroidism in 10·0%. Different kinds of anaemia were found in 11·7% of the patient cases and 10·6% had additional chronic venous insufficiency or post-thrombotic syndrome (Table 3).

Primary diagnoses of patient cases with pyoderma gangrenosum as the secondary diagnosis

The most frequent primary diagnosis of the 985 patient cases with PG as the secondary diagnosis was chronic leg ulcers in 7·5% of the patient cases. This was followed by cardiovascular problems such as atherosclerosis in 6·1% and heart failure in 2·9% and various skin diseases such as erysipelas (4·1%), phlegmon (1·4%), bacterial abscess (1·5%) and purpura (0·9%) as primary diagnoses. Ulcerative colitis was present in 3·3% and Crohn's disease in 2·9% of the patients with PG. Lymphomas (mature T/NK-cell) were found in 1·1% (Table 4).

Discussion

In our study, we describe the worldwide largest cohort of patient cases with PG reported so far. In total, we analysed the DRG data of 1227 inpatient cases with PG as the primary diagnosis and 985 cases with PG as the secondary diagnosis. In both groups, the ratio of women to men was 2:1 and the most often registered age was 75–79 years. These epidemiological data are comparable with other investigations. Next to well-known comorbidities such as IBD, lymphoproliferative disorders and autoimmune diseases, our evaluation indicates more comorbidities such as aspects of the metabolic syndrome (1,7,8).

Pathophysiology and corresponding therapy

The aetiology of PG is not completely understood. There is emerging evidence that PG is not an isolated disease of the skin, but rather a systemic inflammatory disease with an abnormal T-cell response and increased levels of tumor necrosis factor (TNF)-α, interleukin (IL)-1 and IL-6 (11,12). Similar effects of pro-inflammatory cytokines are described for immune-mediated inflammatory diseases (IMID) such as psoriasis and IBD so that comparable therapeutic strategies including TNF-α antibodies have been recently applied (13). The TNF-α-related chronic inflammatory diseases (TRECID) are known to be associated with pre-diabetic metabolism, atherosclerosis and an increasing number of cardiovascular events (14).

A recently published German multicentre study with 259 PG patients evaluated the cofactors and comorbidities of this rare disease. The study described an association between metabolic/endocrinological disease and PG. In detail, 25·5% of the patients suffered from NIDDM and 11·2% from thyroid disorders (1). A similar tendency was found in a single-centre investigation in our dermatological department with 49 patients of whom 38·8% had an endocrine disease, 28·6% had diabetes mellitus and 32·6% were obese. Based on these findings, it was proposed that a possible causal association exists between PG and metabolic syndrome (15). On the basis of our new analysis, the association between PG and metabolic syndrome could be confirmed. Besides arterial hypertension in half of the cases, NIDDM was found in 25·1%, obesity in 8·6% and a disorder of lipid metabolism in 10·8% of the patients. In our data set, 94·8% of all cases showed relevant factors of metabolic syndrome. Compared with the normal adult German population aged between 19 and 79 years, arterial hypertension (50·3% versus 29·7% in men; 26·9% in women) and NIDDM (25·1% versus 4·7% in men; 5·6% in women) were found to be increased in PG cases by >20% [16]. Moreover, obesity was noticed more often in males with PG (32·6%) than in males without PG (19·1%) and in females (21·2%) (16). Unexpectedly, hyperlipidaemia was found in >60% of the German population (64·5% men; 65·7% women) but only in 10·8% of the cases with a PG. This could have been caused by a coding bias in the DRG system, in which hyperlipidaemia represents a less relevant parameter for case severity and, thus, may not always be documented. In contrast, other classic comorbidities, which have been suggested in the past, seem to be less associated with PG in our data set, at least for patients in Germany. Powell et al. suggested a

Table 3 Comorbidities of patient cases with pyoderma gangrenosum as the primary diagnosis

ICD code	Count 2012 ($n=1227$)	%	Diagnosis
I10	617	50·3	Essential hypertension
B96	528	43·0	Other bacteria (*Mycoplasma, Escherichia coli, Pseudomonas*)
B95	487	39·7	Streptococci and Staphylococci
E11	308	25·1	Diabetes mellitus type 2
Z92	258	21·0	Anamnestic medical treatment (Phenprocoumon, radiation, chemotherapy)
E87	205	16·7	Other disorders of water and electrolyte metabolism (acidosis, alkalosis, hyperpotassaemia, hypopotassaemia)
N18	183	14·1	Chronic renal failure
I48	175	14·3	Atrial fibrillation, atrial flutter
D50-67	143	11·7	Anaemia
U80	142	11·6	Antibiotic-resistant pathogens (Staphylococci, Streptococci, Enterococci, Pseudomonas)
Z74	137	11·2	Problems with care support (mobility, personal care)
I25	137	11·2	Chronic ischaemic heart disease
R52	135	11·0	Pain
E78	133	10·8	Disorder of the lipid metabolism (hypercholesterolaemia, hyperlipidaemia)
I87	130	10·6	Venous diseases (post-thrombotic syndrome, venous insufficiency)
I50	125	10·2	Heart failure
E03	123	10·0	Hypothyroidism
Z88	123	10·0	Anamnestic drug allergy
I70	120	9·8	Atherosclerosis
Z29	214	9·3	Necessity of prophylactic measure (isolation, chemotherapy)
E66	106	8·6	Obesity
M06	64	5·2	Other chronic polyarthritis
K50	55	4·5	Crohn's disease
F17	54	4·4	Smoking
K51	51	4·2	Ulcerative colitis
M05	14	1·1	Seropositive chronic polyarthritis

Table 4 Primary diagnoses of patient cases with pyoderma gangrenosum as the secondary diagnosis

ICD code	Count 2012 ($n=985$)	%	Diagnosis
L97	74	7·5	Chronic leg ulcer
I70	60	6·1	Atherosclerosis
I83	41	4·2	Varicose of the lower extremities
A46	40	4·1	Erysipelas
E11	38	3·9	Diabetes mellitus type 2
K51	33	3·4	Ulcerative colitis
K50	29	2·9	Crohn's disease
I50	29	2·9	Heart failure
A41	22	2·2	Other sepsis
L98	18	1·8	Other skin disease
L02	15	1·5	Skin abscess
L03	14	1·4	Phlegmons
N17	12	1·2	Acute renal failure
J18	12	1·2	Pneumonia
M31	9	0·9	Necrotic vasculopathy
T81	7	0·7	Surgical complications
N18	7	0·7	Chronic renal failure
K57	7	0·7	Diverticulosis of the intestine
M05	7	0·7	Seropositive chronic polyarthritis
D69	5	0·5	Purpura

high association of PG to inflammatory diseases, for example, 33·0% of PG patients in the USA suffered from concurrent arthrosis and 36·0% from IBD (1,7). Similar results were published by Binus et al. They found an association of PG patients with arthrosis in 19·4% and with IBD in 34·0% in Boston (17). Al Ghazal *et al.* showed that gastrointestinal diseases (chronic active hepatitis 4·2%, ulcerative colitis 6·6%, Crohn's disease 2·7%, diverticulosis 3·5%, others 8·5%) were codiagnosed in 25·5%, arthropathies in 18·5% and haematological diseases in 3·9% of German PG patients (1). These findings could be confirmed by the current official data as 4·5% of the patient cases had Crohn's disease, 4·1% had ulcerative colitis, 5·2% had arthropathies and 4·0% had lymphoproliferative disorders (Table 3). Solid and haematological neoplasms were also registered in most of the other studies implying that PG is repeatedly discussed as a potential paraneoplastic phenomenon (1,7,8,17).

Primary diagnoses of patient cases with pyoderma gangrenosum as the secondary diagnosis

The primary diagnosis recorded most frequently in association with PG as the secondary diagnosis was leg ulcers (L97·0) in 7·5%, without providing additional details on the pathophysiological cause. One explanation could be the possibility of a false diagnosis because PG is most often located on the lower leg (7). It is likely that PG is not detected in every patient properly because of the lack of worldwide generally accepted criteria for the definite diagnosis (Table 5). PG is a difficult-to-diagnose disease with numerous differential diagnoses (18,19). Another explanation is that therapists coded the symptom as the primary diagnosis and the underlying reason for the wound as the secondary diagnosis. This kind of coding inpatients is still allowed for the German DRG system. The remaining spectrum of primary diagnoses in the DRG data

Table 5 Diagnostic criteria for pyoderma gangrenosum as described in the literature (3,5,22)

Major criteria
Typical clinical presentation: sterile pustule or painful ulcer with livid, undermined wound border
Exclusion of relevant differential diagnoses: chronic venous/arterial leg ulcer, vasculitis, vasculopathies, Martorell's ulcer, cancer
Minor criteria
Typical histopathological presentation: neutrophilic infiltration of the dermis with vasculitis and accumulation of immunoglobulins and/or complement factors around vessels
Association with concomitant diseases: bowel diseases, arthropathies, haematological disorders, neoplasms, endocrine dysfunctions, metabolic syndrome
Fast response to immunosuppressive therapy or no response to conventional wound therapy
Pathergy phenomenon

set included atherosclerosis in 6·1%, varicosis of the lower extremities in 4·2% and other skin disease in 1·8% of the cases. These diseases could be discussed as additional triggering factors for PG and might explain the predilection site for the lower leg. The expected and often described gastrointestinal disorders were found in 6·3% and arthropathies in rarely 0·6% of the cases. As a risk factor of the metabolic syndrome, NIDDM was coded in 3·9%, which was also coded as the secondary diagnosis in 25·1% of the cases (Table 3).

Although the diagnosis of PG is considered as difficult among physicians of different specialisations, our data evaluation suggests an overall increase in the diagnosed cases from 790 cases in 2005 to 1227 cases in 2012. A possible reason for this observation might be an increasing awareness of this orphan disease in the scientific literature, for example, in the context of TRECID.

Sex and age of the patients

Epidemiological data regarding patients' gender and age are very heterogeneous in the literature. Some authors described a more or less equal frequency of PG in both genders (1,3,8,15) while others reported a 2:1 or 3:1 ratio of women to men (5,17). Together with our present observation, we suggest that PG occurs more often in women: a phenomenon underlining the theory of an autoimmune disease, which affects a majority of women. The reason for that disproportion is still unclear, but women are known to respond to infection, vaccination and trauma with increased antibody production and a more T-helper (Th)2-predominant immune response, whereas a Th1 response and inflammation are usually more severe in men. This might be an effect of the influence of sex hormone on the autoimmune system (20–22).

The reported mean age for patients with PG in the literature is 30–60 years, but even children could be affected in rare cases (23,24). However, in our DRG data set, we observed a considerably higher peak in age. The most frequently registered age was 75–79 years for both groups, when a classification in 5-year intervals was applied (n = 192 cases with PG as the primary diagnosis; n = 176 with PG as the secondary diagnosis).

The populations that have been described in other analyses were aged between 2 and 94 years, with an average mean age between 48·4 (8) and 59·7 years (15). We could also observe that the age of the patients with PG as the primary diagnosis, similar to in the other groups, moved upwards from 65–69 years (2005–2007) over 70–74 years (2008–2011) to 75–79 years (2012) over the years according to the demographic transitions in Germany.

Limitations

The analysis of DRG data is, however, limited in different ways. First, there are several options to encode medical diagnoses and, second, there is no possibility to prove the correctness of diagnoses in retrospect. This implies that there might be patients with a well-diagnosed PG that was coded, for example, as a chronic leg ulcer L97.0 or otherwise. Moreover, the identification of PG is difficult so that patients can be coded with other diseases because PG was not correctly diagnosed. On the other hand, there is also the risk of bias of over-diagnosing PG as few cases mentioned here do not potentially have PG (25).

Another concern is that the DRG data do not reflect individual patients, but rather patient cases. Therefore, it is possible that some patients are registered more than once over the years. Finally, the coded secondary diagnoses have some restrictions, because only the relevant ones for the current documented inpatient stay are registered. This results, for example, in a potential gap of neoplastic underlying disease if they were not relevant or treated in the documented inpatient stay.

Conclusion

This epidemiological study describes the worldwide largest population with PG or ulcerations coded as PG and confirmed a wide range of potentially relevant partly not yet described comorbidities and cofactors such as the metabolic syndrome. Further in-depth knowledge on concurrent diseases may improve our understanding of the underlying pathophysiology and identification of persons with elevated risks.

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References

1. Al Ghazal P, Herberger K, Schaller J, Strölin A, Hoff NP, Goerge T, Roth H, Rabe E, Karrer S, Renner R, Maschke J, Horn T, Hepp J, Eming S, Wollina U, Zutt M, Sick I, Splieth B, Dill D, Klode J, Dissemond J. Associated factors and comorbidities in patients with pyoderma gangrenosum in Germany: a retrospective multicentric analysis in 259 patients. *Orphanet J Rare Dis* 2013;**8**:136.
2. Wollina U. Pyoderma gangrenosum – a review. *Orphanet J Rare Dis* 2007;**2**:19.
3. Powell FC, Su WP, Perry HO. Pyoderma gangrenosum: classification and management. *J Am Acad Dermatol* 1996;**34**:395–409.
4. Brunsting LA, Goeckerman WH, O'Leary PA. Pyoderma [ecthyma] gangrenosum: clinical and experimental observations in five cases occurring in adults. *Arch Dermatol Syph* 1930;**22**:655–80.

5. Von den Driesch P. Pyoderma gangrenosum: a report of 44 cases with follow-up. *Br J Dermatol* 1997;**137**:1000–5.
6. Crowson AN, Mihm MC, Magro C. Pyoderma gangrenosum: a review. *J Cutan Pathol* 2003;**30**:97–107.
7. Powell F, Schroeter A, Su W, Perry H. Pyoderma gangrenosum: a review of 86 patients. *Q J Med* 1985;**55**:173–86.
8. Bennett M, Jackson J, Jorizzo J, Fleischer A, White W, Callen J. Pyoderma gangrenosum. a comparison of typical and atypical forms with an emphasis on time to remission. Case review of 86 patients from 2 institutions. *Medicine (Baltimore)* 2000;**79**:37–46.
9. Langan SM, Groves RW, Card TR, Gulliford MC. Incidence, mortality, and disease associations of pyoderma gangrenosum in the United Kingdom: a retrospective cohort study. *J Invest Dermatol* 2012;**132**:2166–70.
10. Schuch V, Moysidis T, Santosa F, Kröger K. Dementia and amputation. *Interv Med Appl Sci* 2012;**4**:175–80.
11. Coady K. The diagnosis and treatment of pyoderma gangraenosum. *J Wound Care* 2000;**9**:282–5.
12. Müller-Ladner U, Alten R, Heiligenhaus A, Kekow J, Koletzko S, Mrowietz U, Ochsenkühn T, Radke M, Reich K, Rudwaleit M, Schreiber S. "TRECID", TNFalpha related chronic inflammatory diseases - a new multiple diseases bridging concept. *Dtsch Med Wochenschr* 2009;**134**:2132–6.
13. Hurwitz RM, Haseman JH. The evolution of pyoderma gangraenosum. a clinicopathologic correlation. *Am J Dermatopathol* 1993;**15**:28–33.
14. von Hundelshausen P, Weber C. Chronic inflammation and artherosclerosis. *Dtsch Med Wochenschr* 2013;**138**:1839–44.
15. Al Ghazal P, Körber A, Klode J, Dissemond J. Untersuchung neuer Kofaktoren bei 49 Patienten mit Pyoderma gangrenosum. *J Dtsch Dermatol Ges* 2012;**10**:251–7.
16. Bergmann KE, Mensink GBM. Körpermaße und Übergewicht. Der Bundes-Gesindheitssurvey 1998. Das Gesundheitswesen. Schwerpunkt zum Gesundheitssurvey 1998. *Das Gesundheitswesen* 1999;**61**:S115–120.
17. Binus AM, Qureshi AA, Li VW, Winterfield LS. Pyoderma gangrenosum: a retrospective review of patient characteristics, comorbidities, and therapy in 103 patients. *Br J Dermatol* 2011;**165**:1244–50.
18. Su WP, Davis MD, Weenig RH, Powell FC, Perry HO. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. *Int J Dermatol* 2004;**43**:790–800.
19. Weenig RH, Davis MD, Dahl PR, Su WP. Skin ulcers misdiagnosed as pyoderma gangrenosum. *N Engl J Med* 2002;**347**:1412–8.
20. De Fairweather L, Frisancho-Kiss S, Rose NR. Sex differences in autoimmune disease from a pathological perspective. *Am J Pathol* 2008;**173**:600–9.
21. Jacobson DL, Gange SJ, Rose NR, Graham NM. Epidemiology and estimated population burden of selected autoimmune diseases in the United States. *Clin Immunol Immunopathol* 1997;**84**:223–43.
22. Moroni L, Bianchi I, Lleo A. Geoepidemiology, gender and autoimmune disease. *Autoimmun Rev* 2012;**11**:386–92.
23. Glass AT, Bancila E, Milgraum S. Pyoderma gangrenosum in infancy: the youngest reported patient. *J Am Acad Dermatol* 1991;**25**(1 Pt 1):109–10.
24. Powell FC, Perry HO. Pyoderma gangrenosum in childhood. *Arch Dermatol* 1984;**120**:757–61.
25. Hafner J, Nobbe S, Partsch H, Läuchli S, Mayer D, Amann-Vesti B, Speich R, Schmid C, Burg G, French LE. Martorell hypertensive ischemic leg ulcer: a model of ischemic subcutaneous arteriolosclerosis. *Arch Dermatol* 2010;**146**:961–8.