8 Cleaver N, Ramirez J, Gildenberg S. Cutaneous lupus erythematosus in a patient undergoing intravitreal bevacizumab injections: case report and review of the literature. *J Drugs Dermatol* 2013; **12**:1052–5.
9 Stollar BD, Stephenson F. Apoptosis and nucleosomes. *Lupus* 2002; **11**:787–9.
10 Keisner SV, Shah SR. Pazopanib: the newest tyrosine kinase inhibitor for the treatment of advanced or metastatic renal cell carcinoma. *Drugs* 2011; **71**:443–54.

Funding sources: none.

Conflicts of interest: none declared.

Tattoos and coincidental skin conditions: the example of lymphomatoid papulosis

DOI: 10.1111/bjd.13120

Dear Editor, I read with interest the recent report by Haus *et al.*[1] about a patient who developed two lesions of lymphomatoid papulosis (LyP) on the red parts of a tattoo. However, their report deserves a few comments. Many reported pseudolymphomas on tattoos involve T cells or both T and B cells, and are not attributed 'mainly' to B cells, as described in the manuscript.[2,3] To date, Sangueza *et al.*[4] in 1992 have published the only well-documented report of the malignant transformation of a T-cell pseudolymphoma into a monoclonal B-cell lymphoma related to a chronic tattoo reaction.

It is widely accepted that mercury has disappeared from red ink manufacturing.[5] Despite withdrawal of mercury, red tattoo reactions, including pseudolymphoma, still occur, raising the question of the culprit component or by-product leading to such reactions. Beyond the nosological issues that the authors try to discuss (LyP or pseudolymphoma), the present case illustrates an increasingly frequent situation due to the popularity of tattoos, namely the occurrence of coincidental dermatological conditions in tattooed individuals. Indeed, in the vast majority of cases of both pseudolymphoma and other 'allergic' reactions, tattoos display either a complete infiltration of the whole culprit colour or an infiltration made by more or less distinct papules or nodules restricted to one colour.[2,3] A tattoo 'allergy' does not present as one, two or three single lesions on a very little part of the culprit colour. It is hard to conceive that a chronic stimulation of a clonal subset of lymphocytes against a specific component of the colour would be responsible for only an extremely limited reaction on two distant parts of such a wildly coloured area as reported by Haus *et al.* Besides, despite being rare, localized LyP happens more often among the young.[6]

It seems rather likely that this patient developed a localized LyP on a fortuitous tattooed area. One could argue the possible presence of specific impurities located specifically on both areas that could have selected a monoclonal population, but it is pushing the speculation rather far, especially as the reaction spontaneously resolved after 2 months and the patient has now been disease free for the past 1·5 years. Pseudolymphomas on tattoos may indeed regress spontaneously,[2] but they usually follow a protracted course in the absence of any treatment. The number of anecdotal reactions on tattoos[7] will keep on increasing with the popularity of tattoos and the ageing of the tattooed population, due to a fortuitous coexistence of a skin condition and the tattoo. LyP on a tattoo seems to be one of them.

N. Kluger

Department of Dermatology, Allergology and Venereology, Institute of Clinical Medicine, University of Helsinki, and Skin and Allergy Hospital, Helsinki University Central Hospital, Meilahdentie 2, P.O. Box 160, FIN-00029 HUS, Helsinki, Finland
E-mail: nicolaskluger@yahoo.fr

References

1 Haus G, Utikal J, Geraud C *et al.* CD30-positive lymphoproliferative disorder in a red tattoo: regional lymphomatoid papulosis type C or pseudolymphoma? *Br J Dermatol* 2014; **171**:668–70.
2 Kluger N, Vermeulen C, Moguelet P *et al.* Cutaneous lymphoid hyperplasia (pseudolymphoma) in tattoos: a case series of seven patients. *J Eur Acad Dermatol Venereol* 2010; **24**:208–13.
3 Marchesi A, Parodi PC, Brioschi M *et al.* Tattoo ink-related cutaneous pseudolymphoma: a rare but significant complication. Case report and review of the literature. *Aesthetic Plast Surg* 2014; **38**:471–8.
4 Sangueza OP, Yadav S, White CR Jr, Braziel RM. Evolution of B-cell lymphoma from pseudolymphoma. A multidisciplinary approach using histology, immunohistochemistry, and Southern blot analysis. *Am J Dermatopathol* 1992; **14**:408–13.
5 Forte G, Petrucci F, Cristaudo A, Bocca B. Market survey on toxic metals contained in tattoo inks. *Sci Total Environ* 2009; **407**:5997–6002.
6 Hsu YJ, Su LH, Hsu YL *et al.* Localized lymphomatoid papulosis. *J Am Acad Dermatol* 2010; **62**:353–6.
7 Kluger N. Cutaneous complications related to permanent decorative tattooing. *Expert Rev Clin Immunol* 2010; **6**:363–71.

Funding sources: none.

Conflicts of interest: none declared.

Association of hidradenitis suppurativa disease severity with increased risk for systemic comorbidities

DOI: 10.1111/bjd.13122

Dear Editor, Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic, inflammatory skin disease affecting terminal hair follicles in apocrine-gland-bearing skin.[1]

Table 1 Baseline status of enrolled patients with hidradenitis suppurativa (HS)

		HS severity	
	All patients, n = 154	High disease burden, n = 60	Medium disease burden, n = 94
Demographics			
Age (years), mean ± SD	36·3 ± 11·76	37·2 ± 12·90	35·8 ± 11·00
Age < 40 years, n (%)	98 (63·6)	37 (62)	61 (65)
Female, n (%)	110 (71·4)	35 (58)	75 (80)
Race, n (%)			
White	110 (71·4)	42 (70)	68 (72)
Black	29 (18·8)	12 (20)	17 (18)
Other	15 (9·7)	6 (10)	9 (10)
Characteristics			
Nicotine use, n (%)			
Ever used	108 (70·1)	44 (73)	64 (68)
Current user	85 (55·2)	40 (67)	45 (48)
Former user	23 (14·9)	4 (7)	19 (20)
Nonuser	46 (29·9)	16 (27)	30 (32)
Body weight (kg), mean ± SD	97·2 ± 24·80	100·1 ± 27·61	95·4 ± 22·79
BMI (kg m^{-2}), mean ± SD	34·0 ± 8·56	34·9 ± 9·72	33·5 ± 7·75
BMI 30–40, n (%)	58 (37·7)	17 (28)	41 (44)
BMI > 40, n (%)	43 (27·9)	22 (37)	21 (22)
Blood pressure (mmHg), systolic/diastolic, mean ± SD	125 ± 13·9/79 ± 1·0	125 ± 14·2/79 ± 9·6	125 ± 13·9/80 ± 10·2
HS disease duration (years), mean ± SD	11·9 ± 9·52	12·0 ± 9·11	11·8 ± 9·82
Family history of HS, n (%)	43 (27·9)	20 (33)	23 (24)
HS-PGA, n (%)			
Moderate or less	105 (68·2)	11 (18)	94 (100)
Severe/very severe	49 (31·8)	49 (82)	0
Hurley stage, n (%)			
I/II (mild/moderate)	109 (70·8)	15 (25)	94 (100)
III (severe/very severe)	45 (29·2)	45 (75)	0
Prior therapies/medications, n (%)			
Topical	76 (49·4)	30 (50)	46 (49)
Systemic	151 (98·1)	58 (97)	93 (99)
hsCRP[a] (mg L^{-1}), mean ± SD	17·5 ± 26·02 (n = 117)	32·7 ± 36·79 (n = 43)	8·7 ± 9·09 (n = 74)
VAS skin pain score,[b] mean ± SD	54·3 ± 26·46	65·9 ± 24·64	46·8 ± 24·96
PHQ-9 score[c] (0–27), mean ± SD	9·5 ± 6·69 (n = 153)	11·0 ± 6·49	8·5 ± 6·66 (n = 93)
Modifiable cardiovascular risk factors			
History of diabetes mellitus, n (%)	10 (6·5)		
Current tobacco use, n (%)	85 (55·2)		
BMI ≥ 30 and/or obesity, n (%)	103 (66·9)		
TC ≥ 240 mg dL^{-1} or medical history of hyperlipidaemia, n (%)	18 (11·7)		
SBP ≥ 140 and/or DBP ≥ 90 mmHg or history of hypertension, n (%)	39·6 (61·0)		
Number of risk factors, n (%)			
2	55 (35·7)		
3	28 (18·2)		
4	7 (4·5)		
5	2 (1·3)		

Percentages are based on patients with nonmissing values. BMI, body mass index; DBP, diastolic blood pressure; hsCRP, high-sensitivity C-reactive protein; HS-PGA, HS Physician's Global Assessment; PHQ, Patient Health Questionnaire; SBP, systolic blood pressure; TC, total cholesterol; VAS, visual analogue scale. [a]Normal range < 3·1 mg L^{-1}. [b]VAS ranging from 0 (no pain) to 100 (worst pain). [c]PHQ-9 scores for depression severity: 0–4 none, 5–9 mild, 10–14 moderate, 15–19 moderately severe, 20–27 severe.

Associated comorbidities include depression,[2] obesity[3] and metabolic syndrome.[4] The objective of the current analysis of patients with moderate-to-severe HS was to identify the most common comorbidities, their prevalence according to the level of HS disease burden (high vs. medium) and any association between baseline characteristics and the risk for the comorbidity. These patients, representing one of the largest HS groups to be evaluated to date, were adults from a 52-week, phase 2, randomised, double-blind, placebo-controlled trial of adalimumab treatment,[5] who had at least moderate disease [HS Physician's Global Assessment (HS-PGA) grade ≥ 3; 0–5 scale]. Additional inclusion/exclusion criteria were published previously.[5]

Baseline comorbidities were identified with patient reports and medical histories. The following conditions were defined: hypertension, use of antihypertensive medication and/or self-reported history; uncontrolled hypertension, systolic/diastolic blood pressure (SBP/DBP) ≥ 140/≥ 90 mmHg; depression, Patient Health Questionnaire 9 (PHQ-9) score ≥ 10;[6] morbid obesity, body mass index (BMI) ≥ 40 kg m^{-2}; hyperlipidaemia, total cholesterol ≥ 240 mg dL^{-1}; high HS disease burden, HS-PGA > 3 and/or Hurley stage III; and medium HS disease burden, HS-PGA ≤ 3 and Hurley stage II.[5]

All patients with available baseline values were included in this analysis. All statistical tests were two-sided and significant at 0·05. Associations between the most common comorbidities and baseline characteristics were evaluated by logistic regression. The odds ratio (OR) with 95% Wald confidence interval (CI) was provided. Final models were chosen by stepwise selection with a P-value of 0·15 for both entry and stay. Model selection was conducted per Akaike information criteria and Bayesian information criteria, which confirmed the final models selected by the stepwise selection method.

Of the 154 patients in this analysis, 60 (39·0%) had high HS disease burden and 94 (61·0%) had medium burden. Mean high-sensitivity C-reactive protein (CRP) was almost four times higher in the high vs. medium disease burden groups (32·7 mg L^{-1} vs. 8·7 mg L^{-1}). Combining self-report and medical examination results, 39·6% of patients had

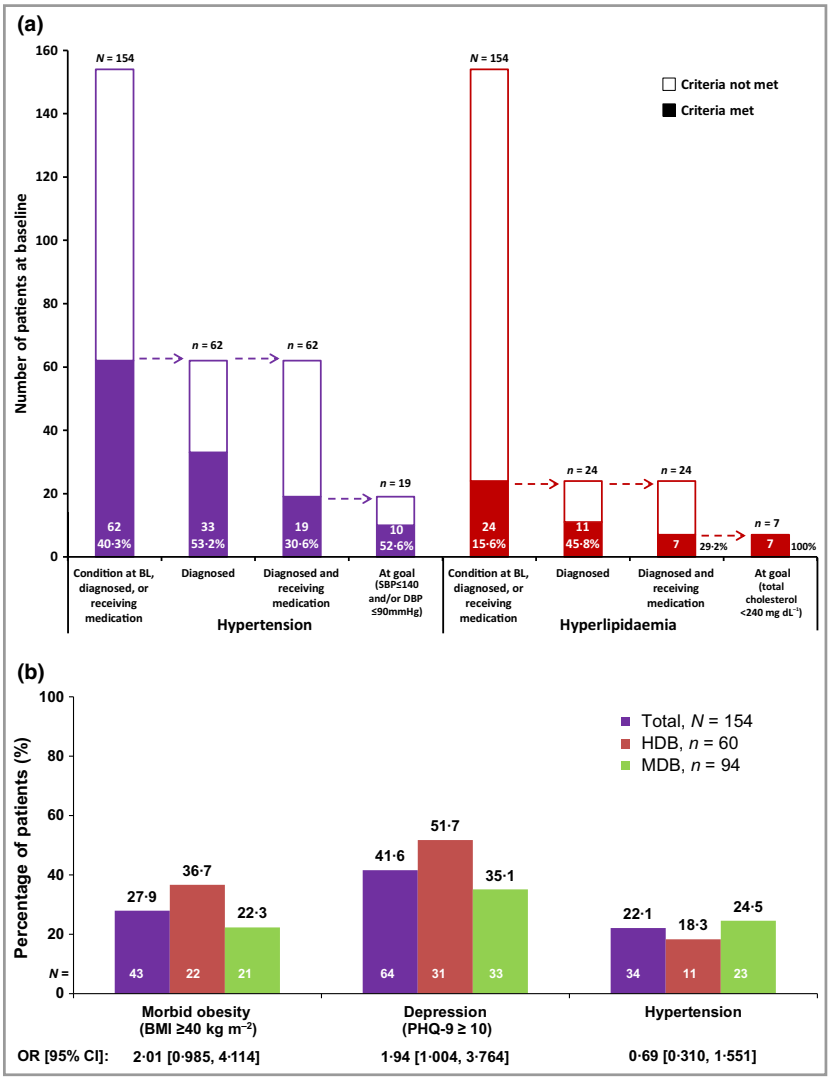

Fig 1. Comorbidities in patients with hidradenitis suppurativa: study population. (a) Number and percentage of patients with hypertension or hyperlipidaemia at baseline (BL). (b) Prevalence of main comorbidities in patients with high disease burden (HDB) vs. medium disease burden (MDB). Hypertension was identified by treatment with antihypertensive medication and/or self-reported history at BL. BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; OR, odds ratio; PHQ, Patient Health Questionnaire; SBP, systolic blood pressure.

hypertension, 38·3% were morbidly obese and 48·1% had depression. The incidence of modifiable cardiovascular risk factors (Table 1) revealed that > 50% of patients were smokers, overweight or had hypertension. Other cardiovascular risk factors included hyperlipidaemia (11·7%) and diabetes mellitus (6·5%). Over one-third of patients (35·7%) had two cardiovascular risk factors (Table 1).

Of the 40·3% of patients who had and/or were diagnosed with hypertension, or were receiving antihypertensive medication (Fig. 1a), 53% had been diagnosed with hypertension, and 31% had been both diagnosed and treated. Of the latter, 53% had reached the treatment goal (SBP/DBP < 140/ < 90 mmHg). Similarly, a minority with hyperlipidaemia were both diagnosed and receiving medication (Fig. 1a).

The percentage of patients with morbid obesity or depression was 14% and 17% higher, respectively, in patients with high vs. medium disease burden (Fig. 1b). The percentage of patients with hypertension was 6% lower in patients with high vs. medium disease burden (Fig. 1b).

Multiple logistic regression identified the most influential factors for morbid obesity and depression. An association with increased odds of morbid obesity was seen for high HS disease burden (OR 2·13, 95% CI 1·00–4·53), and a trend towards association was seen for depression (OR 1·74, 95% CI 0·82–3·68). Smoking was associated with reduced odds of morbid obesity (OR 0·47, 95% CI 0·22–0·99). High HS disease burden (OR 2·12, 95% CI 1·04–4·31), female sex (OR 2·57, 95% CI 1·13–5·85) and smoking (OR 2·35, 95% CI 1·15–4·81) were associated with increased odds of depression.

High HS disease burden was significantly associated with increased prevalence of morbid obesity and depression, but not hypertension, partially contradicting a previous report that also demonstrated the high prevalence of obesity and depression in patients with HS, but not significant association between disease severity and BMI or depression.[7] Our findings are novel because we demonstrate that the magnitude of HS disease burden appears to be correlated with the risk of depression and morbid obesity, even after controlling for possible confounding variables.

Based on these findings, instructive parallels and differences can be drawn between HS and psoriasis. Positive correlations between psoriasis disease severity and obesity[8] and between psoriasis disease severity and CRP elevation[9] have been demonstrated. However, patients with psoriasis have lower CRP levels,[9] and psoriasis disease severity correlates with hypertension prevalence.[8] More than just skin diseases, both HS and psoriasis are systemic diseases associated with high systemic inflammation and numerous comorbidities.

This analysis had several limitations. A cross-sectional study cannot assess causality. This population may not reflect the entire spectrum of patients with HS because it was limited to clinical trial participants, for whom previous treatment with tumour necrosis factor-α inhibitors, cardiac insufficiency (New York Heart Association class III or greater), active skin diseases and tumours were exclusion criteria.[9] Meaningful correlations were difficult to establish due to the limited population size. Finally, patient-reported prevalence of comorbidities is subject to recall bias.

Acknowledgments

The authors would like to thank Jody Bennett, employee of AbbVie, for assistance in writing the first draft of this publication.

[1]*Bakersfield Dermatology, 5101 Commerce Drive, Bakersfield, CA 93309, U.S.A.*
[2]*Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands*
[3]*Departments of Dermatology, Venereology, Allergology and Immunology, Dessau Medical Center, Dessau, Germany*
[4]*Weill Cornell College of Medicine, New York, NY, U.S.A.*
[5]*Harvard Medical School, Boston, MA, U.S.A.*
[6]*AbbVie Inc., North Chicago, IL, U.S.A.*
[7]*Florida Academic Dermatology Center, Miami, FL, U.S.A.*
E-mail: crowley415@aol.com

J.J. Crowley[1]
J.R. Mekkes[2]
C.C. Zouboulis[3]
N. Scheinfeld[4]
A. Kimball[5]
M. Sundaram[6]
Y. Gu[6]
M.M. Okun[6]
F. Kerdel[7]

References

1 Fimmel S, Zouboulis CC. Comorbidities of hidradenitis suppurativa (acne inversa). *Dermatoendocrinol* 2010; **2**:9–16.
2 Onderdijk AJ, van der Zee HH, Esmann S *et al.* Depression in patients with hidradenitis suppurativa. *J Eur Acad Dermatol Venereol* 2013; **27**:473–8.
3 Revuz JE, Canoui-Poitrine F, Wolkenstein P *et al.* Prevalence and factors associated with hidradenitis suppurativa: results from two case–control studies. *J Am Acad Dermatol* 2008; **59**:596–601.
4 Sabat R, Chanwangpong A, Schneider-Burrus S *et al.* Increased prevalence of metabolic syndrome in patients with acne inversa. *PLoS ONE* 2012; **7**:e31810.
5 Kimball AB, Kerdel F, Adams D *et al.* Adalimumab for the treatment of moderate to severe hidradenitis suppurativa: a parallel randomized trial. *Ann Intern Med* 2012; **157**:846–55.
6 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; **16**:606–13.
7 Vazquez BG, Alikhan A, Weaver AL *et al.* Incidence of hidradenitis suppurativa and associated factors: a population-based study of Olmsted County, *Minnesota. J Invest Dermatol* 2013; **133**:97–103.
8 Neimann AL, Shin DB, Wang X *et al.* Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol* 2006; **55**:829–35.
9 Coimbra S, Oliveira H, Reis F *et al.* C-reactive protein and leucocyte activation in psoriasis vulgaris according to severity and therapy. *J Eur Acad Dermatol Venereol* 2010; **24**:789–96.

Funding sources: AbbVie Inc. funded this study and participated in the study design, data collection, data management, data analysis and preparation of the manuscript. All authors had full access to the data and were involved in the analysis of data, development and revision

of the manuscript, and decision to submit the manuscript for publication.

Conflicts of interest: J.J.C. has received honoraria and grants from AbbVie and Amgen for participation on ad boards and as a speaker and investigator, and grants from Astra-Zeneca, Celgene, Janssen, Lilly, Pfizer, Merck and Regeneron for participation as an investigator. J.R.M. declares no conflicts of interest; his department was reimbursed by AbbVie for his participation as an investigator in this clinical trial. C.C.Z. has received honoraria from AbbVie and Stiefel/GlaxoSmithKline for participation on advisory boards, and as an investigator and speaker; from Galderma for participation on advisory boards; from LEO Pharma for participation as a consultant; and from Bayer Health Care, Bioderma, Biogen-Idec, General Topics and Glenmark for his participation as a speaker; his department received grants from AbbVie, Biogen-Idec, BMS, Immundiagnostik AG, LVMH, Merz, Pierre Fabre and UCB for his participation as an investigator, and from Intendis for his participation on an advisory board. N.S. has received payments from AbbVie and Celgene for participation as an investigator; honoraria from Medicis, Merz, Stiefel and Valeant for participation on advisory boards; and receives a salary as an employee of Optigenex, Inc. A.K. is a consultant and investigator for Janssen, AbbVie and Amgen, and has received fellowship funding from Janssen. F.K. has received honoraria from AbbVie, Amgen, Astellas, Galderma, Janssen and Medicis for participation as a speaker; and has received grants from AbbVie for participation as an investigator. M.S., Y.G. and M.M.O. receive a salary as AbbVie employees, and may also receive AbbVie stock, stock options and/or stock grants.

Some data from this manuscript were presented at the 71st Annual Meeting of the American Academy of Dermatology (AAD) at Miami Beach, FL, U.S.A., 1–5 March 2013.

Familial pachyonychia congenita with steatocystoma multiplex and multiple abscesses of the scalp due to the p.Asn92Ser mutation in keratin 17

DOI: 10.1111/bjd.13123

Dear Editor, Pachyonychia congenita (PC) is a rare genodermatosis transmitted as an autosomal dominant trait that is caused by mutations in the differentiation-specific keratin genes *KRT6a* (52%), *KRT6b* (3%), *KRT16* (28%) or *KRT17* (17%), which are expressed in the nails, skin, oral mucosa, larynx, hair and teeth.[1] Approximately 1000 patients with PC have been identified, of whom 400 have been confirmed genetically to have it. Two subtypes have been classically described: PC-1 (Jadassohn–Lewandowsky type, OMIM#167200), caused by mutations in *KRT6a* or *KRT16*, with predominant oral leucokeratosis and palmoplantar keratoderma; and PC-2 (Jackson–Lawler type, OMIM#167210) resulting from mutations in *KRT6b* or *KRT17*, with neonatal teeth, pili torti and multiple cysts.[2,3] The presence of multiple sebaceous cysts [steatocystoma multiplex (SM)] at puberty has been proposed to differentiate PC-2 from PC-1,[2,3] but it is now recognized that there is a considerable overlap between the two classical subtypes of PC, and a new classification based on the mutated keratin gene has now been proposed (PC-6a, PC-6b, PC-16 and PC-17).[4,5]

A 12-year-old girl presented with a painful inflammatory plaque on her scalp, which had appeared recently without any fever. She had a previous history of microcysts on her face and multiple unsuccessful treatments for suspected fungal infection of fingernails and toenails. She had neonatal teeth. Her mother had multiple steatocystomas on her face and trunk (Fig. 1a), focal plantar keratoderma (Fig. 1b), normal nails and a history of neonatal teeth. She had no history of abscesses. Clinical examination of the scalp of the proband showed multiple suppurative, well-circumscribed, alopecic and cicatricial plaques on her vertex (Fig. 2a) and rough hair. She had multiple microcysts on her face, predominantly on her forehead (Fig. 2b); sebaceous cysts in the armpits; ophryogenes-type keratosis pilaris of the eyebrows; pachyonychia of all finger and toenails (Fig. 2c); and keratosis pilaris on both thighs. The patient had no palmoplantar keratoderma. Histology of the scalp revealed a cystic formation with no content, lined with a thin eosinophilic epithelial lining, highly suggestive of a sebaceous cyst (Fig. 2d). A non-perifollicular polymorphic inflammatory granuloma, rich in neutrophils, lymphocytes and plasmocytes, was seen in the deep dermis. Fungal examination was negative, and bacteriological cultures yielded occasional colonies of *Staphylococcus aureus*. Microscopical examination of the hair shaft showed normal thickness and a longitudinal fissure giving a flat appearance (in places triangu-

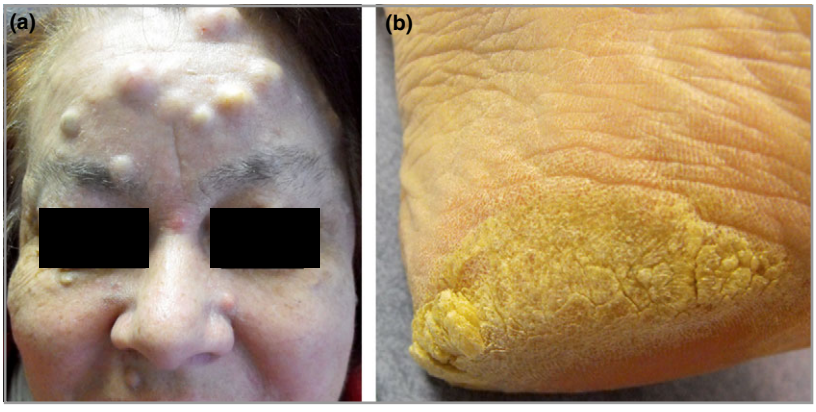

Fig 1. Clinical features of the patient's mother. (a) Multiple steatocystomas of the face predominating on the forehead. (b) Focal plantar keratoderma of the heel.