Dermatol Ther (Heidelb) (2017) 7:167–174
DOI 10.1007/s13555-017-0173-6

CASE REPORT

A Report of Two Cases of Solid Facial Edema in Acne

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Received: July 12, 2016 / Published online: February 6, 2017

ABSTRACT

Introduction: Solid facial edema (SFE) is a rare complication of acne vulgaris. To examine the clinical features of acne patients with solid facial edema, and to give an overview on the outcome of previous topical and systemic treatments in the cases so far published.
Methods: We report two cases from Switzerland, both young men with initially papulopustular acne resistant to topical retinoids.
Results: Both cases responded to oral isotretinoin, in one case combined with oral steroids. Our cases show a strikingly similar clinical appearance to the cases described by Connelly and Winkelmann in 1985 (Connelly MG, Winkelmann RK. Solid facial edema as a complication of acne vulgaris. Arch Dermatol. 1985;121(1):87), as well as to cases of Morbihan's disease that occurs as a rare complication of rosacea.
Conclusion: Even 30 years after, the cause of the edema remains unknown. In two of the original four cases, a potential triggering factor was identified such as facial trauma or insect bites; however, our two patients did not report such occurrencies. The rare cases of solid facial edema in both acne and rosacea might hold the key to understanding the specific inflammatory pattern that creates both persisting inflammation and disturbed fluid homeostasis which can occur as a slightly different presentation in dermatomyositis, angioedema, Heerfordt's syndrome and other conditions.

Keywords: Adrenergic receptors; Brimonidine; Erythema; Rosacea; Vasoconstriction; Worsening of erythema

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INTRODUCTION

Acne vulgaris is a disorder of the pilosebaceous unit, namely the sebaceous gland and the hair follicle it is attached to. Some 85% of people have acne at some point in their life, especially during puberty [1], and therefore it could be considered the most common inflammatory skin disease. Due to disfiguration and scarring, the disease has major effects on the patient's quality of life [2], eliciting depression, social

withdrawal, anxiety and a higher rate of unemployment [3, 4].

The pathogenesis includes several components whose interplay is only partially known. The androgen surge in puberty stimulates the sebocytes and follicular keratinocytes that proliferate and obstruct the outflow tract of the hair follicle. This leads to a hyperplasia of the sebaceous glands and the seborrhea that is characteristic for acne. *Propionibacterium acnes*, an opportunistic grampositive anaerobic strain found in the seborrheic areas of the skin, breaks down fatty acids. These compounds are believed to elicit inflammation and chemotaxis of neutrophil granulocytes and adaptive immune cells to the follicular epithelium. This ends in the rupture and release of sebum, microorganisms and keratin into the dermis. Accumulation of neutrophils, lymphocytes and foreign-body giant cells leads to the characteristic erythematous papules, pustules, nodules and cysts of inflammatory acne [1, 5].

In very rare cases, however, the primary acne lesions occur together with a wooden, solid facial edema (SFE). Typically, the acne lesions are moderate to severe but in no way extreme, hence this phenomenon cannot be explained by simple edema due to inflammation. It was first observed and published by Connelly and Winkelmann in 1985 [6]. Although we believe we have understood more about acne pathogenesis since then, solid facial edema remains a mystery. It has been suggested that chronic inflammation, comparable to other body regions such as the legs, damages the lymphatic system and leads to fibrosis, which is further supported by mast cells. Accordingly, early treatment before damage is irreversible seems sensible. Here, we report two Swiss cases of SFE in acne vulgaris and summarize the clinical features and treatment responses of SFE cases in the literature.

Case Report

A 18-year old carpenter presented with numerous papules and pustules on the forehead and cheeks compatible with acne. Initially, he had been fruitlessly treated with topical retinoids. Instead, after 6 months of therapy, the patient developed a localized, symmetric, wooden, non-pitting edema over the cheeks and infraorbital regions, the lower front and glabella. All edematous areas were beset with multiple comedones and papulopustules (Fig. 1). A punch biopsy revealed some dermal edema and fibrosis as well as moderate infiltrates composed of lymphocytes and neutrophils granulocytes around the pilo-sebaceous unit (Fig. 2). Treatment with 2 mg/kg oral prednisone for 12 days in combination with 20 mg isotretinoin for 2 months resulted in a complete regression of the edema.

The second case was an otherwise healthy 20-year-old student, who consulted for a persisting edematous reaction of the left upper and lower eyelid and cheek that had developed 5 months earlier. It had started during treatment with topical retinoids for erythematous papules and pustules interpreted as acne vulgaris that had arisen on the forehead, cheeks, chin and pre-sternal area. Shortly after commencing the treatment, the indurated edema developed. No comedones nor teleangiectasias were present. A biopsy showed a spongiotic dermatitis, probably due to local treatment, as well as acne of a typical mixed cellular and

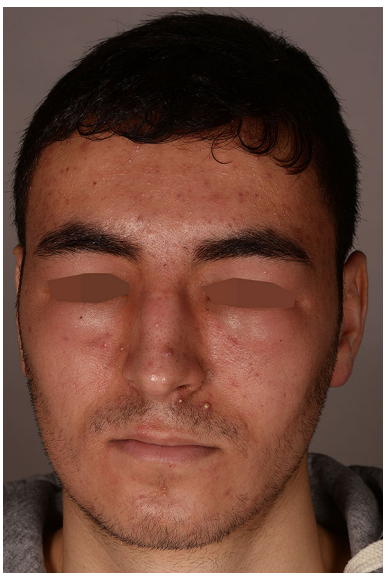

Fig. 1 Diffuse papules and pustules with facial wooden edema in the periorbital area

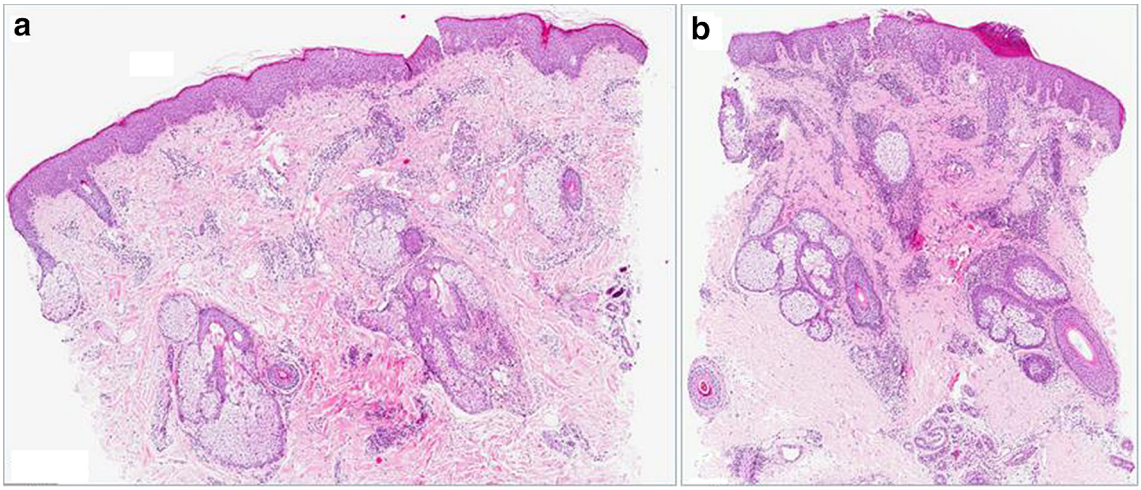

Fig. 2 Biopsy of case 1 revealing dermal edema and fibrosis as well as mixed cellular infiltrate around the pilo-sebaceous unit

mixed perifollicular inflammation. Further, fibrosis in the middle and dermis was quite prominent. After 8 months treatment with isotretinoin 20 mg per day and an antihistamine, the facial edema slowly cleared.

Compliance with Ethics Guidelines

Informed consent was obtained from the patients prior to publication.

DISCUSSION

A total of 20 similar cases have been reported so far in the medical literature (Table 1). Multiple strategies were used in attempts to treat the edema. The first therapy attempt, with elastic facial stockings for several months as reported by Connelly and Winkelmann, failed [6]. In 8 cases, 0.5–1 mg/kg per day isotretinoin was reported as an effective treatment of the facial edema in acne vulgaris [7–10]. There were two reported cases of treatment failure after 3 and 4 months of therapy with isotretinoin, which corresponds with our experience, as in the second case, we observed improvement only after 8 months of treatment [11, 12]. Therapy attempts with oral prednisone alone showed no improvement of the facial edema, in contrast to successes by a combination with isotretinoin [13]. Surgical therapy after failure of conventional treatment, as reported in one case, led to complete resolution [14]. It remains unknown whether the result was aesthetically satisfying. In the related condition called Morbihan disease, isotretinoin monotherapy and combination therapies of isotretinoin with either ketotifen or clofazimine all produced good results [12, 15].

These two cases illustrate this typical, almost unmistakable, disease of solid facial edema which produces a striking facies. This condition does not stand alone—clinically closely comparable to the initial report of Connelly and Winkelmann [6], quite similar reports of SFE as a rare complication of rosacea (Morbihan disease) were published in 1957 [15]. Morbihan disease also produces solid facial edema with histopathologic features of granulomatous rosacea that can occur at any stage of the disease [15]. The pathogenesis of Morbihan disease also remains unclear [15, 16], the two main hypotheses being lymph vessel abnormalities or the edema representing an inflammatory effect [12, 15]. This peculiar edema is not reduced when standing, nor does it show variation during the day. Interestingly, a number of other facial dermatoses can produce similar effects, including dermatomyositis, angiedema, Melkersson–Rosenthal and Heerfordt's syndrome [17–19].

We believe a common inflammatory pattern may be underlying all these conditions. A

Table 1 Cases of SFE reported in the literature

Case No.	Location	Age (years)	Sex	History of acne	Acne lesions	Trigger of edema	Delay until presentation (years)	Treatment	Success	References
1	Face	20	M	For 8 years	Papulopustules, nodules, hemorrhagic crusts, comedones and atrophic scars confined to the face	Unknown	2	4 months of isotretinoin (0.5 mg/kg/day) and 4 months of ketotifen (2 mg/day)	Complete resolution	[10]
2	Face	18	M	For 6 months	Papules and pustules on the forehead and cheeks	Topical retinoids	0.1825	Oral prednisone 2 mg/kg/day for 12 days in combination with isotretinoin 20 mg for 2 months	Complete resolution	This report
3	Face	20	M	For 8 months	Papules and pustules on the forehead, cheeks and chin	Topical retinoids	0.125	8 months treatment with isotretinoin 20 mg/day and antihistamine	Complete resolution	This report
4	Face	65	M	Acne as a child and 'cysts all his life'	Facial biopsy compatible with sebaceous hyperplasia and rosacea	Unknown	4	Surgery (debulking of the affected tissue) after failure of conventional treatment	Complete resolution	[14]
5	Face	20	M	For 3 years, no treatment	Moderate juvenile polymorphic acne	Unknown	2	8 months of isotretinoin 1 mg/kg/day	50% reduction	[7]
6	Face	15	F	Unknown	Nodular pustules in the right nasolabial fold	Unknown	1	6 months of isotretinoin 1 mg/kg/day	80% reduction	[7]

Table 1 continued

Case No.	Location	Age (years)	Sex	History of acne	Acne lesions	Trigger of edema	Delay until presentation (years)	Treatment	Success	References
7	Face	17	M	Moderate papulocystic acne for 3 years	Facial lesions consisting of inflammatory papules and scattered pustules and cysts	Unknown	1	20 weeks of isotretinoin (40 mg/twice a day = 1.0 mg/kg/day)	Moderate reduction	[9]
8	Face	20	F	Acne vulgaris for 4 years	Unknown	Unknown	0.33	20 weeks of isotretinoin (30 mg/day) and clofazimine (100 mg four times a week), manual lymph drainage once a week for 15 times	Moderate reduction	[8]
9	Face	18	M	Acne for 4 years	Numerous inflammatory acne lesions	Unknown	0.75	Isotretinoin (50 mg/day for 12 weeks, 40 mg/day for 12 weeks), manual lymph drainage for two weeks	Moderate reduction	[8]
10	Face	21	W	Nodulocystic acne for 5 years	Erythematous, solid, edematous plaques and firm, deep-seated nodules on the cheeks and forehead	Unknown	NA	Injections of hot water into the indurated areas, typhoid fever therapy and X-ray treatment	Moderate reduction	[6]
11	Face	18	M	Papulopustular acne vulgaris	Unknown	Unknown	NA	Systemic steroid therapy	Moderate reduction	[20]

Table 1 continued

Case No.	Location	Age (years)	Sex	History of acne	Acne lesions	Trigger of edema	Delay until presentation (years)	Treatment	Success	References
12	Mid-face	24	M	For 10 years	Erythematous papules with few pustules across the cheeks and nose	Unknown	1.5	3 months of isotretinoin 1 mg/kg/day and 1 month of prednisone	No	[21]
13	Face	25	M	For 11 years	Multiple pitting scars on the whole face but no inflammatory acne lesions	Unknown	4	2 months of oral tetracyclines 500 mg and 4 months isotretinoin (40 mg/day = 0.5 mg/kg)	No	[11]
14	Face	18	M	Papulopustular acne for 3 years	Excoriated papular acne lesions on the forehead and upper part of the back	Unknown	0.75	15 months of elastic facial stockings	No	[6]
15	Face	20	M	For 3 years	Papular acne on the chin, acne scarring on the forehead	Motor vehicle accident	2	15 months of elastic facial stockings	No	[6]
16	Face	20	M	For 2 years	Papulopustular acne on the forehead	Gnat bite	0.5	6 weeks of oral corticosteroids	No	[6]
17/18	Face	14	M	For 1 year	Severe papulopustular acne, primarily involving the face, associated with pronounced centrofacial edema	Unknown	0.25	Betamethasone 1.5 mg/day, stopped after 2 weeks due to inefficacy. Oral and topical antibiotics	Persistence of edema, resolution of acne	[22]

Table 1 continued

Case No.	Location	Age (years)	Sex	History of acne	Acne lesions	Trigger of edema	Delay until presentation (years)	Treatment	Success	References
19	Face	18	M	Unknown	Intense papulopustular acne without scarring and seborrheic dermatitis	Unknown	NA	Prednisone (20 mg/day)	Unknown	[13]
20	Face	17	M	Unknown	Seborrheic dermatitis and papulopustular acne	Unknown	2	Prednisone (15 mg/day)	Unknown	[13]

number of mediators are directly involved in induction of edema, including bradykinin, interleukin 1 beta, histamine and others. These are produced by cells both of the innate (mast cells, granulocytes, monocytes/macrophages) as well as of the adaptive immune system (T cells). We have therefore undertaken comparative studies that are currently ongoing. Once the pathogenesis of persisting edema is better understood, more targeted and effective therapies might be within our reach.

ACKNOWLEDGEMENTS

No funding or sponsorship was received for this study or publication of this article. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

Disclosures. Sarah Kuhn-Régnier, Joanna Mangana, Katrin Kerl, Jivko Kamarachev, Lars E. French, Antonio Cozzio and Alexander A. Navarini have nothing to disclose.

Compliance with Ethics Guidelines. Informed consent was obtained from the patients prior to publication.

Data Availability. All data generated or analyzed during this study are included in this published.

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