DERMATOLOGICA SINICA 31 (2013) 102–103

Contents lists available at SciVerse ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

CORRESPONDENCE

Neutrophilic sebaceous adenitis responsive to oral isotretinoin

Dear Editor,

Neutrophilic sebaceous adenitis (NSA) was initially described in dogs, with an unclear etiology. Only three human cases have been reported.[1–3] We reported another case in an Asian man, who responded well to oral isotretinoin.

The 38-year-old man had suffered from erythematous plaques with satellite papules on bilateral cheeks for 3 months. The lesions started as discrete reddish papules, which gradually enlarged into confluent annular plaques with elevated borders (Figure 1A and B). The rashes were asymptomatic initially, but became mildly pruritic on the margins. He went to another hospital and was diagnosed with *Demodex* infestation after biopsy. He received 1 week of oral metronidazole, but the facial plaques still persisted. We obtained the previous biopsy and performed another biopsy on the edge of the annular plaque. A review of the previous biopsy showed neutrophil aggregation, with scattered necrotic sebocytes in the sebaceous lobules (Figure 2A). The basal layer of sebaceous glands appeared intact without damage by neutrophils and the dense neutrophils appeared to be surrounding the sebaceous glands with little infiltration (migration) through the lobules (Figure 2A). One *Demodex* was present in the sebaceous lobule (Figure 2A). In addition, dense lymphocytic and scattered eosinophilic infiltrations were present around the pilosebaceous units, with nearly no involvement in hair follicle epithelium (Figure 2B). Our biopsy showed similar histopathologic features without the presence of *Demodex* on serial sections. NSA was diagnosed.

Oral indomethacin was given for 2 weeks without effect. We then prescribed 4 weeks of oral isotretinoin, 40 mg/day for the first 2 weeks and 20 mg/day for the next 2 weeks. The patient's facial

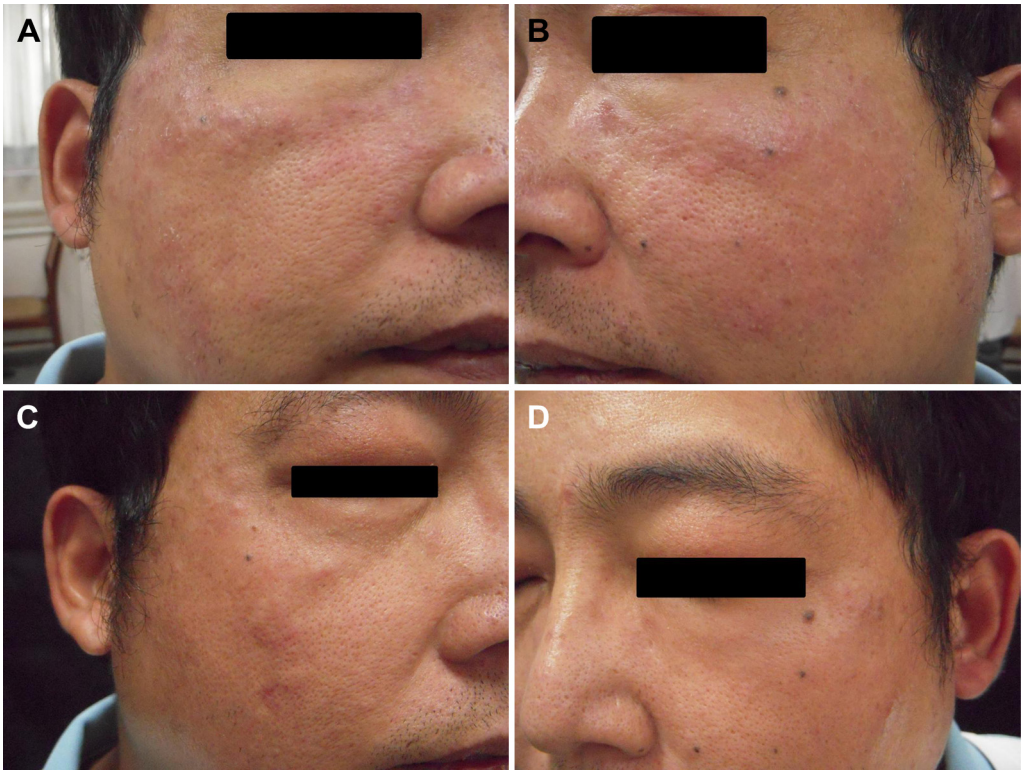

Figure 1 Multiple reddish papules and plaques arranged in annular shape with elevated borders and fine scales on bilateral cheeks: (A) right cheek; (B) left cheek. There were fewer reddish lesions on bilateral cheeks after oral isotretinoin treatment: (C) right cheek; (D) left cheek..

http://dx.doi.org/10.1016/j.dsi.2012.06.008

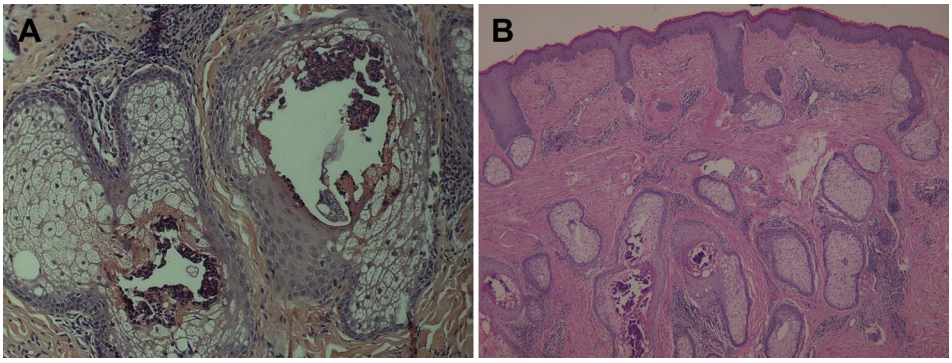

Figure 2 (A) Inflammatory cell aggregation within the sebaceous gland and necrosis of sebocytes leading to foci of glandular vacuolization. *Demodex* infest ation in one of the sebaceous lobules (hematoxylin-eosin stain, ×100); (B) multifocal inflammatory infiltrations with perivascular and interglandular distribution. There was nearly no involvement of the hair follicle epithelium (hematoxylin-eosin stain, ×40).

erythema subsided completely and no recurrence was noted 6 months after the end of treatment (Figure 1C and D).

NSA was initially described in humans by Renfro et al as a sebaceous gland disorder on the face.[1] NSA clinically manifests as annular erythematous plaques with elevated borders. Histopathology shows neutrophilic aggregates in the sebaceous lobules and scattered necrotic sebocytes.[1] Neutrophils may be absent in the late stage andlymphohistiocytic cells may surround the perisebaceous epithelium.[2] The mechanism of NSA is still uncertain. NSA is considered as a photodermatosis in a case report in Spain, with seasonal recurrences after sun exposure.[3]

Sebaceous adenitis has also been reported in different species of dogs, and is characterized by multifocal annular erythematous plaques and alopecia with scaling change.[4] Several veterinary journals speculated the possible pathogenesis of sebaceous adenitis in dogs as the following: (1) a primary structural defect in sebaceous glands or ducts, that results in the leakage of sebum and subsequent development of a foreign body inflammatory response; (2) an immune-mediated or autoimmune reaction; (3) a defect of keratinization, leading to sebaceous duct obstruction; or (4) an abnormality of lipid metabolism.[4] Currently, sebaceous adenitis is believed to be an immune-medicated disease[5] and presents a genetic characterization with significantly less minor mtDNA haplotypes in studies in Standard Poodles in the US and the UK.[6]

Differential diagnoses of NSA include Ofuji's disease and demodicidosis on the face. Unlike the neutrophil aggregation in the sebaceous lobules of neutrophilic sebaceous adenitis, Ofuji's disease is characterized by eosinophil infiltrations in the follicles and in the follicular orifices. Ofuji's disease typically appears as a follicular area of erythematous papules and pustules, which could gradually become confluent, creating indurate polycyclic plaques with a healing center and a spreading periphery. Ofuji's disease also responds favorably to oral indomethacin, which produced no response in our patient. *Demodex* may be a normal habitant in the pilosebaceous unit, but cutaneous demodicidosis could be diagnosed by the presence of more than five mites/cm^2 in a standardized skin surface biopsy. We performed serial sections of the biopsy sample and there was only one *Demodex* found in the sebaceous lobules. Besides, the clinical condition of the patient did not improve after oral metronidazole treatment. Thus, we considered Ofuji's disease and demodicidosis as a less likely diagnosis in our case.

NSA may remit spontaneously, but therapeutic experience of NSA is limited in humans. However, several therapies of sebaceous adenitis have been proposed in dogs, such as oral cyclosporine A or vitamin A.[7]

NSA as a new entity needs further investigation into the correct etiopathogenesis. Although discussion of the possible mechanism of isotretinoin could be speculation, our patient achieved long term remission after oral isotretinoin treatment. The beneficial effect of oral isotretinoin in achieving long-term remission in our patient may be explained by: (1) the sebostatic effects of isotretinoin in shrinking sebaceous glands, inhibiting the differentiation of mature sebocytes[8]; (2) apoptosis and cell cycle arrest in human sebaceous gland cells induced by isotretinoin[8]; and (3) the anti-inflammatory effects of isotretinoin.

NSA may be an underreported disease in humans. We reported our experience in an Asian male who responded well to oral isotretinoin. More investigations are needed to identify the pathogenesis of NSA.

There were no sources of funding for this work.

Wei-Ting Chou
Department of Dermatology, Show-Chwan Memorial Hospital, Taiwan, ROC

Tsen-Fang Tsai
Department of Dermatology, National Taiwan University Hospital, Taiwan, ROC

Wang-Cheng Ko, Chih-Ming Hung, Yu-Fu Chen*
Department of Dermatology, Show-Chwan Memorial Hospital, Taiwan, ROC

* Corresponding author. Department of Dermatology, Show-Chwan Memorial Hospital, No. 542, Section 1, Chung-Shang Road., Changhua, Taiwan, ROC. Tel.: +886 4 7256166x81212; fax: +886 4 7236226.
E-mail address: b001089101@tmu.edu.tw (Y.-F. Chen),

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Received: Mar 16, 2012
Revised: Jun 20, 2012
Accepted: Jun 21, 2012