

SHORT COMMUNICATION

Naevus Comedonicus Syndrome Complicated by Hidradenitis Suppurativa-like Lesions Responding to Acitretin Treatment

Ge Qian^{1,2#}, Tao Liu^{2##}, Chongchen Zhou¹ and Yinghui Zhang¹Departments of Dermatology, ¹Zhengzhou Children's Hospital, Zhengzhou, and ²Tangdu Hospital, The Fourth Military Medical University, No. 569 Xinsi Road, 710038 Xi'an, China. E-mail: morlab2@fmmu.edu.cn[#]These authors contributed equally to this work and should be considered as first authors.

Accepted Mar 3, 2015; Epub ahead of print Mar 10, 2015

Naevus comedonicus (NC) was first described by Kofmann in 1895 (1). It is characterized by a linear arrangement of dilated follicular openings filled with dark keratinous material. In general, aggressive treatment of NC is not a reasonable approach, except for aesthetic reasons or in special cases. When NC is associated with cataracts, skeletal defects, or central nervous system abnormalities, it is called naevus comedonicus syndrome (NCS) (2–4). We describe here a female patient with NCS complicated by multiple hidradenitis suppurativa (HS)-like lesions that showed a substantial response to oral acitretin in combination with topical adapalene.

CASE REPORT

A 19-year-old woman was first referred to our hospital for evaluation of extensive areas of dilated follicular openings with keratinous plugs localized on her face shortly after birth, which gradually worsened over time. During her childhood, new lesions had extended to nearly all sites of the body except for the hands, feet and nails, as well as mucous membranes with different sized depressed scars. During adolescence, she began to experience recurrent and intolerable painful nodules, abscesses, intercommunicating sinus tracts and hypertrophic scars involving her axillary regions, groin and mons pubis. These lesions relapsed or aggravated during hot weather. Compared with normal children, there was a significant developmental delay, with poor vision developing from the age of 6 years. Her parents reported poor performance at school. In 2013, physical

examination showed a systematized linear pattern of multiple comedones with numerous black dots measuring 1–4 mm in diameter on her shoulders, arms, trunk, buttocks and legs, with perilesional atrophy preponderantly involving the face, scalp, neck and back (Fig. 1). An irregular hairless patch measuring 20 × 8 cm was found on the vertex of the scalp, composed of aggregated atrophic pits plugged with keratinous material, resulting in a classic sieve-like appearance (Fig. 1c). Inflammatory nodules, ulcers, band-like cicatricial contractures in intertriginous regions and absence of hair in the axillary and pubic areas were noted (Fig. 1b, d). Family history and routine laboratory studies were unremarkable. The patient had undergone cataract surgery of the right eye at the age of 13 years. Ophthalmic examination showed horizontal nystagmus and a vision of 2/6 in both eyes. There were lenticular opacities in the left eye. She had scoliosis with spina bifida from C2 to C7, as documented by computed tomography (CT) scan. Histopathological examination showed dilated and invaginated follicular structures filled with lamellar keratin. Based on these findings, a diagnosis of NCS was made. The HS-like lesions involving the intertriginous areas were taken as being secondary to the NC.

Before the age of 6 years, she did not receive any therapeutic modalities except for emollients and moisturizers. Subsequently, topical tretinoin, salicylic acid and vitamin D₃ ointment were applied with no beneficial effect. At puberty, oral and topical antibiotic agents were added because of the development of painful HS-like lesions with abscesses and deep-seated sinus tracts. Relapses after stopping medications were common, with a mean recurrence rate of 6–7 times a year. At age 15 years, after informed consent about side-effects, including teratogenicity, oral acitretin in daily doses of approximately 0.5 mg/kg combined with antibiotic ointment was given from spring to autumn with an

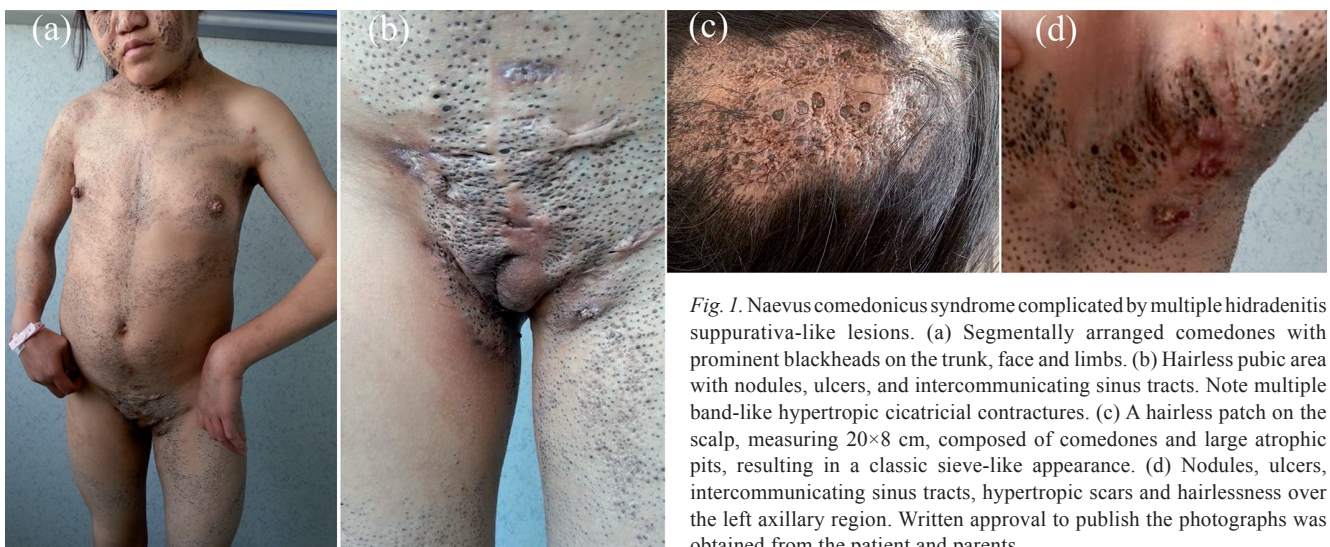


Fig. 1. Naevus comedonicus syndrome complicated by multiple hidradenitis suppurativa-like lesions. (a) Segmentally arranged comedones with prominent blackheads on the trunk, face and limbs. (b) Hairless pubic area with nodules, ulcers, and intercommunicating sinus tracts. Note multiple band-like hypertrophic cicatricial contractures. (c) A hairless patch on the scalp, measuring 20 × 8 cm, composed of comedones and large atrophic pits, resulting in a classic sieve-like appearance. (d) Nodules, ulcers, intercommunicating sinus tracts, hypertrophic scars and hairlessness over the left axillary region. Written approval to publish the photographs was obtained from the patient and parents.

apparent relieving effect. However, the patient declined further therapy despite its obvious effectiveness due to the persistence of retinoid-dermatitis symptoms and an elevation of serum alkaline phosphatase level (> 3 times the upper normal limit). Hence, she only applied topical 0.1% adapalene gel until next spring when new nodular lesions and abscesses reappeared in her groin. Therefore, oral acitretin therapy was added to topical adapalene. During the following 2 years, intermittent seasonal acitretin treatment combined with continuous topical application of adapalene substantially alleviated the burden of HS-like lesions. The mean frequency of inflammatory attacks was reduced from 6–7 times to 1–2 times per year. No severe side-effects, except for retinoid-dermatitis and elevated serum alkaline phosphatase level, were observed, which could be relieved by symptomatic treatment or by stopping the medication.

DISCUSSION

NCS, a term suggested by Engber in 1978 (2), is a multisystem disorder including NC and skeletal, ocular and cerebral abnormalities. The skin lesions are noted at birth or appear shortly thereafter (3, 4). They are characterized by linear groups of dilated, plugged follicular ostia in a honeycomb pattern, which affect the body asymmetrically. The pathogenesis of NCS remains unknown. Although an autosomal mutation that survives by mosaicism has been implicated (5), the genetic basis has yet not been identified. A mutation of a fibroblast growth receptor (FGFR-2), which is exclusively found in epithelial cells including epidermal keratinocytes and sebocytes, might play an important role in the development of NCS (6). In the present case, the systematized involvement of nearly all body areas and the occurrence of HS-like lesions were rather unusual features. Similar inflammatory lesions complicating NC were previously described under the term “HS” or “HS-like lesions” (7). HS is characterized by painful inflamed nodules, abscesses, intercommunicating sinus tracts and hypertrophic scarring in the apocrine gland-bearing areas, most commonly the axillae, inguinal and anogenital regions. Follicular occlusion induced by abnormal follicular development mainly contributes to the aetiology of HS (3). Approximately 90% of HS patients are active smokers or ex-smokers (8), whereas our patient was a non-smoker. It is unclear whether the inflammatory disorder of our patient is identical with classical HS.

As to NC *per se*, the therapeutic options are limited. The most effective, but not always possible or motivated treatment would be complete surgical excision. In

the present case surgical removal of the NC was too widespread for surgical treatment (9–11). In view of the effectiveness of acitretin reported in patients with HS (12), we tentatively started a systemic treatment with this drug. Although continuous therapy with acitretin of 0.5 mg/kg was not well tolerated, an intermittent seasonal treatment combined with continuous topical use of adapalene was effective, with acceptable side-effects. Complete healing of the HS-like lesions, however, could not be achieved. However, further debilitating suppurative disease involving her intertriginous areas would be a reasonable indication for therapy. Hence, surgical removal of the areas affected by HS-like lesions may be envisaged in the future.

The authors declare no conflicts of interest.

REFERENCES

1. Kofmann S. Ein Fall von seltener Localisation und Verbreitung von Comedonen. Arch Dermatol Syphilis 1895; 32: 177.
2. Engber PB. The nevus comedonicus syndrome: a case report with emphasis on associated internal manifestations. Int J Dermatol 1978; 17: 745–749.
3. Pavithra S, Pai H, Mallya H, Pai GS. Nevus comedonicus syndrome. Indian J Dermatol 2011; 56: 771–772.
4. Kaliyadan F, Nampoothiri S, Sunitha V, Kuruvilla VE. Nevus comedonicus syndrome – nevus comedonicus associated with ipsilateral polysyndactyly and bilateral oligodontia. Pediatr Dermatol 2010; 27: 377–379.
5. Happle R. How many epidermal nevus syndromes exist? J Am Acad Dermatol 1991; 25: 550–556.
6. Melnik B, Schmitz G. FGFR2 signaling and the pathogenesis of acne. J Dtsch Dermatol Ges 2008; 6: 721–728.
7. Dufour DN, Bryld LE, Jemec GB. Hidradenitis suppurativa complicating naevus comedonicus: the possible influence of mechanical stress on the development of hidradenitis suppurativa. Dermatology 2010; 220: 323–325.
8. Happle R, König A. Smoker's boils. Dermatology 2011; 222: 282–284.
9. Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. J Am Acad Dermatol 2009; 60: 539–561.
10. Chen YE, Gerstle T, Verma K, Treiser MD, Kimball AB, Orgill DP. Management of hidradenitis suppurativa wounds with an internal vacuum-assisted closure device. Plast Reconstr Surg 2014; 133: 370e–377e.
11. Teo WL, Ong YS, Tan BK. Radical surgical excision and use of lateral thoracic flap for intractable axillary hidradenitis suppurativa. Arch Plast Surg 2012; 39: 663–666.
12. Boer J, Nazary M. Long-term results of acitretin therapy for hidradenitis suppurativa. Is acne inversa also a misnomer? Br J Dermatol 2011; 164: 170–175.