Isotretinoin in acne agminata

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ABSTRACT

Acne agminata is an asymptomatic papulopustular eruption. This condition typically occurs in young adults. The eruption generally runs a self-limited course, but disfiguring scars can occur. Histological examination shows scattered dermal granulomas composed of epitheloid and some giant cells with central caseation. A variety of agents such as wide-spectrum antibiotics, oral steroids, dapsone, and clofazimine have been used with varying degrees of success. Herein, we report 2 Caucasian males with acne agminata, successfully treated with isotretinoin.

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Acne agminata (*Lupus miliaris disseminatus faciei*) consists of an uncommon asymptomatic papulopustular eruption affecting the centrofacial region, occurring predominantly in young adults.[1,2] These papules characteristically are discrete reddish-brown and dome-shaped with a smooth surface, bilaterally distributed in the central muzzle area of the face. This condition tends to run a chronic course of 12-24 months, with spontaneous involution. It is a self-limited condition, however, disfiguring scar formation is a significant cosmetic problem making the patient seek medical attention.[1] Characteristic histopathologic features include scattered dermal granulomas composed of epitheloid and some giant cells, with central caseous necrosis.[2] Aggregates of epithelioid histiocytes and occasional multinucleate giant cells form a substantial tubercle. Sparse lymphoid infiltrates are observed peripherally.[3] Our justification for using isotretinoin in acne agminata was based on its association with acne rosacea, the absence of evidence-based studies supporting other treatments, the risk of scarring, and prior reports of successful isotretinoin treatment. We report 2 cases of acne agminata treated successfully with isotretinoin, preventing severe scar formation and shortening the natural history of the disease.

Case Report. *Patient 1.* A 25-year-old male presented with a 5-month history of a mildly pruritic papular eruption of the face in January 2003. He showed discrete red and gelatinous monomorphic papules of 1-2 mm in diameter, predominantly distributed on the cheeks, upper eyelids, glabella, and forehead (**Figure 1a**). Seborrhea or comedons were not present on examination. He had been previously treated with a combination of oral doxycycline 200 mg/day, topical erythromycin solution and tretinoin cream for 4 months, that was prescribed by his local general practitioner. His condition failed to improve, and the eruption exacerbated. He had no history of tuberculosis. The laboratory findings were all within normal limits: full blood count (FBC), erythrocyte sedimentation rate (ESR), and chest x-ray. His mantoux test was negative. A biopsy specimen taken from one of the papules on the cheek revealed tuberculoid granulomas in the upper and mid-dermis composed of epitheloid cells, and a few giant cells with central caseation necrosis surrounded by round-cell infiltration (**Figure 2**). Staining of the biopsy for acid-fast bacilli was negative. Most of the granulomas were seen around the partially destroyed hair follicles. The clinicopathologic findings were consistent with acne agminata. In February 2003, isotretinoin (Ro-Accutane® capsule, Roche, Switzerland) 40 mg daily (0.6 mg/kg/day) was instituted. Following one month of treatment, there was scaling of individual lesions but no new papules had developed. After 4 months, many of the active papules subsided, leaving depressed

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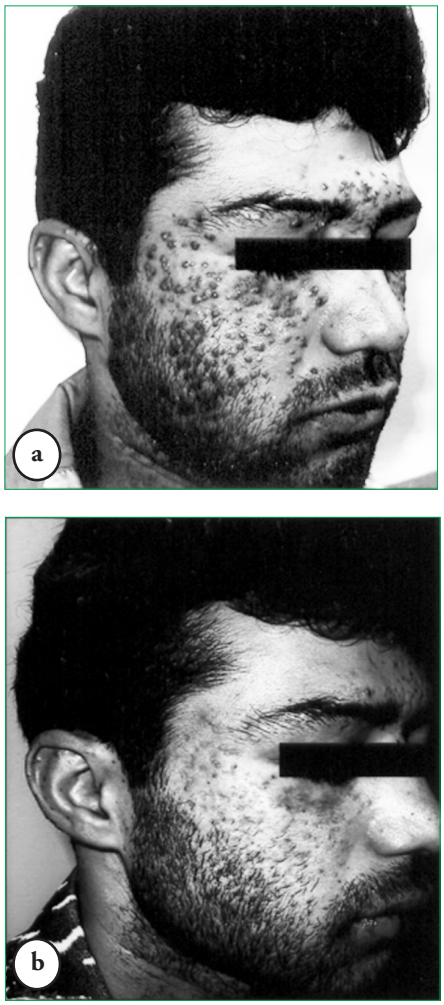

Figure 1 - Patient 1 with **a**) discrete papules of acne agminata before treatment with isotretinoin, **b**) after 6 months of treatment with 0.5 mg/kg per day of isotretinoin. The active papules subsided, leaving few depressed scars.

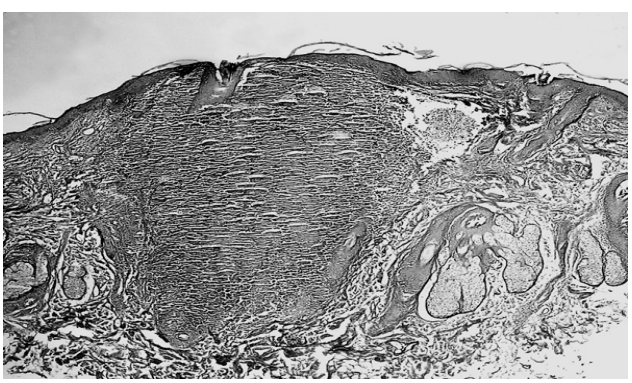

Figure 2 - Biopsy specimen taken from one of the papules (from patient 1), revealed tuberculoid granulomas, composed of epitheloid cells and a few giant cells with central caseation. (Hematoxylin and Eosin staining, original magnification x10).

pitted scars. Isotretinoin was continued for 6 months, and then discontinued while he was almost free of any active papules (**Figure 1b**). No serious adverse-effect was noticed during this therapy. No recurrence was noted at the 6-month follow-up visit.

Patient 2. A 28-year-old male presented with an asymptomatic papular eruption of 6-months duration on his cheeks, upper eyelids, and forehead in May 2001. Examination revealed discrete reddish-brown papules of 1-2 mm in diameter, with a translucent glassy granulomatous appearance, bilaterally involving the face. He had been previously treated with a combination of oral doxycycline 200 mg/day, ketoconazole, clindamycin, and tretinoin for 6 months without any noticeable results. History of tuberculosis was negative. Routine investigations including FBC, ESR, and chest x-ray were normal. A tuberculin skin test was negative (dilution: 0.1). Histology demonstrated epitheloid cells, granulomas in the dermis with central caseation necrosis, and a rim of lymphocytic infiltration encircling the caseation. The specific stain of the biopsy specimen failed to reveal any acid-fast bacilli. The clinicopathologic findings in the absence of sarcoidosis or tuberculosis are consistent with a diagnosis of acne agminata. He was started on isotretinoin (Ro-Accutane capsule, Roche, Switzerland), 40 mg daily (0.5 mg/kg/day). His 4-week visit showed fine scaling over the previous lesions without any recent erupted papules. After 12 weeks, most of the papules had involuted, leaving slight atrophic scars. He was almost free of any active papules, and the cosmetic results were satisfactory. There was no significant side effects on isotretinoin, which was discontinued after 6 months. He had no recurrence of his disease at one-year follow-up.

Discussion. The etiology and pathogenesis of acne agminata have not been clarified yet, therefore a pathophysiologic approach to the treatment and prediction of the therapeutic efficacy of various agents is difficult. The theories supporting the contribution of mites such as *Demodex folliculorum* are not convincing.[4,5] Acne agminata has recently been regarded as a manifestation of papular (granulomatous) type of acne rosacea.[6] However, some authors have put forward acne agminata as a distinctive rosacea-like syndrome and not a granulomatous form of rosacea.[7] There are many contradictory reports of the agents concerned to be effective in the treatment of acne agminata. A number of agents have been used in this condition, but have been reported as variably successful therapy. Oral tetracycline has been used in Japan, but failed to help most of the patients.[1] Minocycline was ineffective, or provided only a temporary improvement.[8] Doxycycline has been reported to be an effective therapy in one patient.[9]

Dapsone has been described to be useful and it appears to shorten the course of the disease.[10] Oral prednisolone is considered to be effective if it is administered early.[8] Recently, clofazimine has been tried in one patient with acne agminata and resulted in a rapid resolution, and sustained remission of the disease.[11]

There is a close similarity of acne agminata and rosacea, and the efficacy of isotretinoin in the treatment of rosacea is well known. Berbis and Privat[12] initiated isotretinoin (Accutane, Roche, Switzerland), 1 mg/kg/day, for a 27-year-old man with acne agminata and observed a marked improvement after 3 months, leaving depressed scars. They tapered the dosage gradually and noted no recurrence one year after withdrawal of the drug. Pharmacologically, isotretinoin is known to influence a wide variety of biological activities responsible for inflammation, and other dysfunctions of pilosebaceous apparatus.[13,14] The recent theories focusing on a central pathogenic role of pilosebaceous apparatus in acne agminata may explain the mechanism of action of isotretinoin in this disease. It further supports the theories regarding acne agminata as a variant of rosacea or a rosacea-like syndrome. Our study revealed that isotretinoin, even with doses as low as 0.5 mg/kg/day may have an effect on both the natural history and eventual resolution of acne agminata. Regarding the fact that acne agminata runs a self-limited course of nearly 2 years without treatment, rapid involution of active papules after a short course of treatment and the sustained remission are in favor of the efficacy of isotretinoin in the alternation of the natural history of acne agminata. In addition, the cosmetic results of treatment with isotretinoin, in comparison with untreated patients suffering from disfiguring scars, is worth mentioning; trivial atrophic scars are the only skin lesions remaining after treatment, however, scarring could have been worse had the patient been left untreated. Adverse effects on the skin and mucous membranes are the most commonly observed side effects of isotretinoin that are generally dose-dependent, and are reversible after cessation of the therapy and treated simply by conservative measures. The more serious side effects such as skeletal defects are usually observed by high-dose and long-term administration of isotretinoin,[14] which was not used in our cases.

This study suggests that in terms of the dramatic clinical results, isotretinoin should be considered as one of the options in the treatment of acne agminata. We instituted isotretinoin for our patients because both of them were resistant to antibiotic therapy, and considered to have severe forms of acne agminata. An issue that remains to be clarified is that isotretinoin may not be justified as the first line treatment for patients with milder forms of acne agminata, because many of them may respond properly to other safer treatments. Dosages as low as 10 mg/day of isotretinoin are considered to be effective in rosacea.[15] It is worth noting that the daily dosage of isotretinoin in our study was lower than that used by Berbis and Privat.[12] Therefore, we suggest further studies to find out the lowest effective dosage feasible for acne agminata.

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