

## Severe Flares of Acne Following Isotretinoin: Large Closed Comedones (Macrocomedones) Are a Risk Factor

Sir,

We report 4 cases of patients with acne vulgaris who, following the commencement of isotretinoin, developed a very severe flare of their acne, causing severe physical and psychological damage. Whilst the flare was most prominent on the face, other sites were involved. In all these cases there were numerous large closed comedones (macrocomedones) located almost solely at the sites where the flare had occurred. All 4 cases were referred from elsewhere and had definitely merited isotretinoin.

*Case 1* was a 27-year-old woman with inflammatory acne vulgaris, initially located almost exclusively on the back. She was commenced on isotretinoin and within one week there had been an abrupt deterioration of her acne, especially on the face (grade 4) (1), where she also had numerous macrocomedones. She was treated with a reduction in the dosage of isotretinoin to  $\frac{2}{3}$  mg kg<sup>-1</sup> and the addition of erythromycin 500 mg twice daily. The large numbers of macrocomedones were treated by repeated ablation with electrocautery after application of EMLA® (2). The patient's condition gradually improved and the isotretinoin was discontinued after 3 months. However, she had developed prominent acne scarring on the face following the acute flare of the acne vulgaris.

*Case 2* was an 18-year-old woman with facial acne who was started on isotretinoin in a dosage of 1 mg kg<sup>-1</sup>. Her acne flared on her face after 3 weeks on isotretinoin and deteriorated to a grade of 2.0; there were also large numbers of macrocomedones on her face. The isotretinoin was discontinued and she was commenced on cyproterone acetate combined with ethinyloestradiol and ciprofloxacin in a dosage of 250 mg 4 times daily. She was also treated with regular electrocautery to the macrocomedones and topical clobetasol propionate to the large inflamed lesions. Her acne improved considerably with a facial grade of 0.25 after 3 months.

*Case 3* was a 27-year-old woman with a 6-year history of acne, located principally on the chest and back. She was started on isotretinoin in a dosage of 0.5 mg kg<sup>-1</sup>. Within 6 weeks there had been a dramatic deterioration in her acne, most notably on the face and back. Associated with the inflamed lesions were numerous macrocomedones. She was treated with a reduction in the dosage of the isotretinoin to 0.25 mg kg<sup>-1</sup> and she was also given erythromycin 500 mg daily. Additionally the macrocomedones were ablated using electrocautery. Both the isotretinoin and erythromycin were continued for a period of 4 months, at the end of which there was no acne at any site. Some minor facial scarring was noted.

*Case 4* was a 24-year-old woman with a 2-year history of acne vulgaris, located principally on the back, who was started on 1.0 mg kg<sup>-1</sup> of isotretinoin. Within 4 weeks there had been an acute flare of her acne on the face, chest and back. A

reduction in the dosage of isotretinoin to 0.5 mg kg<sup>-1</sup> was instituted along with the introduction of erythromycin 500 mg daily. The prominent macrocomedonal component of the acne which was present at all the sites was treated by 2 sessions of ablation. This regime resulted in satisfactory progress, and by 4 months all therapy had been stopped; she had no active acne but did have a moderate degree of scarring.

In the early reports on the action of isotretinoin, a minor flare of acne vulgaris after the institution of isotretinoin was a recognised phenomenon (3). We are aware of only one case report dealing specifically with a flare of cystic acne following the institution of isotretinoin (4), and in the cases the duration of the flare was short, having subsided by the 3rd week with no change of therapy. It has been postulated that when isotretinoin is started the flare seen in acne vulgaris is due to the sudden change in the microenvironment of the *P. acnes* (5), and the subsequent death of large numbers of these organisms causes the release of soluble inflammatory mediators into the circulation. In the cases we describe, the patients had large numbers of non-inflamed macrocomedones that we believe served as a focus for inflammatory mediators, transforming the macrocomedones into inflamed lesions. The cases we describe illustrate that care is required when starting patients on isotretinoin if they have large numbers of macrocomedones, especially when facial. If a severe flare of acne vulgaris has occurred and lasted for more than 2 to 3 weeks after starting isotretinoin we feel that the most effective management is to reduce the dosage of isotretinoin, add a non-tetracycline antibiotic, consider using a potent topical steroid for some of the more inflamed lesions and to look for and treat any macrocomedones by physical ablation, using electrocautery after applying a topical anaesthetic.

### REFERENCES

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