

Familial Marjolin's ulcers in aggressive acne

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Summary

Acne conglobata represents one end of the spectrum of diseases that comprise the entity commonly known as 'acne'. It is a severe form of acne that presents later than typical acne vulgaris and often runs a chronic, unremitting and, often disfiguring, course well into adulthood. Marjolin's ulcers represent well differentiated squamous cell carcinomas that arise in areas of chronic inflammation and scarring. Intense inflammation and scarring are the hallmarks of acne conglobata. We present a family with three of its members afflicted by severe acne conglobata, who each subsequently developed locally aggressive, well differentiated squamous cell carcinomas of the head and neck. Analysis would suggest autosomal dominant transmission.

Introduction

'Acne' represents a diverse set of dermatologic problems along a wide spectrum of disease severity. Amongst the most aggressive forms of acne is acne conglobata. This term is generally applied to a highly inflammatory disease replete with nodules, abscesses, large comedones and the occurrence of draining sinus tracts, affecting primarily the trunk, and to a lesser extent, the head and neck region. Pathologically, one sees a highly inflammatory process that destroys the normal architecture of the skin appendages. Often a dense perifollicular infiltrate is noted. This infiltrate is so concentrated as to commonly form the abscesses, with subsequent draining cutaneous tracts, that are frequently seen in acne conglobata. As with other forms of aggressive acne, the acute inflammatory stages of the disease heal with severe, often whorled scarring,

that is frequently hypertrophic or atrophic in nature. This is a disease primarily of males. Although acne conglobata may uncommonly occur in females, they are often less severely affected than their male counterparts. This form of acne needs to be primarily differentiated from cystic acne vulgaris, since the prognosis is significantly different between the two disease entities. Unlike acne vulgaris, acne conglobata is a disease primarily of young adulthood, not adolescence, and it tends to run a chronic unremitting course. Treatment has been unrewarding. However, several trials have documented some response of acne conglobata to prolonged treatment with isotretinoin¹⁻³.

'Marjolin's ulcers' represent locally invasive aggressive squamous cell carcinomas arising in areas of chronic inflammation and old scarring. Areas of predilection for the development of these tumors have been reported to include: old



Fig. 1. Active cystic, inflammatory acne with numerous comedones.

burn scars, leg ulcers and a discoid type of systemic lupus erythematosus⁴. It is not at all surprising that the severe inflammatory background and scarring that are evident in acne conglobata have been noted to be associated with the unusual development of Marjolin's ulcers. Case reports of Marjolin's ulcers arising in long-standing aggressive acne conglobata have been few in number^{3,5-8}. We present the most recent case of Marjolin's ulcer arising in acne conglobata. This represents the third such case arising in a single family.

Case report

A 36-year-old Caucasian male presented with a history of severe acne conglobata since adolescence. He had severe involvement of the trunk, extremities and head and neck areas with numerous active subcutaneous cysts, abscesses, double comedones and large areas of atrophic and hypertrophic scarring (Fig. 1). Three years prior to presentation, he had suffered a third degree burn to the back of his neck, both axillae and left hand. These areas had subsequently been adequately treated with skin grafting. He presented to us with a five-month history of a rapidly progressive, painless and destructive lesion of his midface (Fig. 2). CT scan confirmed an ulcerating soft tissue mass involving the left paranasal skin, anterior face of maxilla, left nasal bone and inferior aspect of orbit (Fig. 3). There



Fig. 2. Destructive lesion of midface involving nose, orbit and maxilla on left side.

was no evidence of suspicious cervical adenopathy. MRI scanning confirmed that the tumor extended to abut the medial rectus muscle and the anteromedial aspect of the globe. There was no evidence of intracranial extension. A confirmatory biopsy revealed the presence of well differentiated acantholytic squamous cell carcinoma. It was determined that this young and active gentleman's best chance of cure rested with aggressive combined therapy. Thus, he underwent en bloc excision of his lesion, including orbital exenteration, with rectus free flap reconstruction of his subsequent defect (Fig. 4). Orbital aesthetic rehabilitation with osseointegration and other prosthetics was offered to the patient, and refused. The patient's procedure was uneventful. No gross residual tumor was evident at the completion of the extirpation. Post-



Fig. 3. Extensive invasive lesion involving orbit (with displacement of globe), and destroying maxillary framework on left side.



Fig. 4. Resected specimen consisting of orbit, nose and maxilla, patient was reconstructed with a rectus abdominis free flap.

operative radiotherapy was, unfortunately, interrupted on numerous occasions due to the patient's non-compliance. He remains alive and well with no sign of recurrent or persistent disease.

Discussion

This most recent case of Marjolin's ulcer arising from acne conglobata is the third such case in this patient's immediate family. The patient's father had suffered from severe acne conglobata for most of his adult life. He had developed a well-differentiated, highly invasive squamous cell carcinoma in the right lateral aspect of his neck. At the time of surgical extirpation, the tumor was noted to have invaded deeply into his trapezius, scapular, supraspinatus and infraspinatus muscles. Despite extensive resection, the patient succumbed to local persistence of the disease one and a half years later, at the age of 56.

Our patient's older brother had likewise suffered from long-standing severe acne conglobata since adolescence. He, too, developed a very well-differentiated highly invasive squamous cell carcinoma. His tumor arose in the right preauricular area and, again, was noted to be deeply invasive. At the time of surgical resection it was noted to have involved the temporal bone, the sphenoid sinus, the mandible and orbit. Despite aggressive resection and a full course of external beam radiotherapy, the patient succumbed to local persistence of his disease approximately two years later, at the age of 31.

In each case, the squamous cell carcinomas were noted to be very well-differentiated lesions surrounded by areas of dense inflammatory infiltrate. Every member of this family that was affected with severe acne conglobata developed aggressive, locally invasive Marjolin's ulcers of the head and neck. Three of our patient's siblings had relatively mild acne that did not run the chronic unremitting course into adulthood that is so typical of acne conglobata. Their disease likely represented acne vulgaris. One sibling had perfectly clear skin, not having ever suffered from acne of any sort. The pattern of inheritance suggested by analysis of the family tree would be most in keeping with autosomal dominant

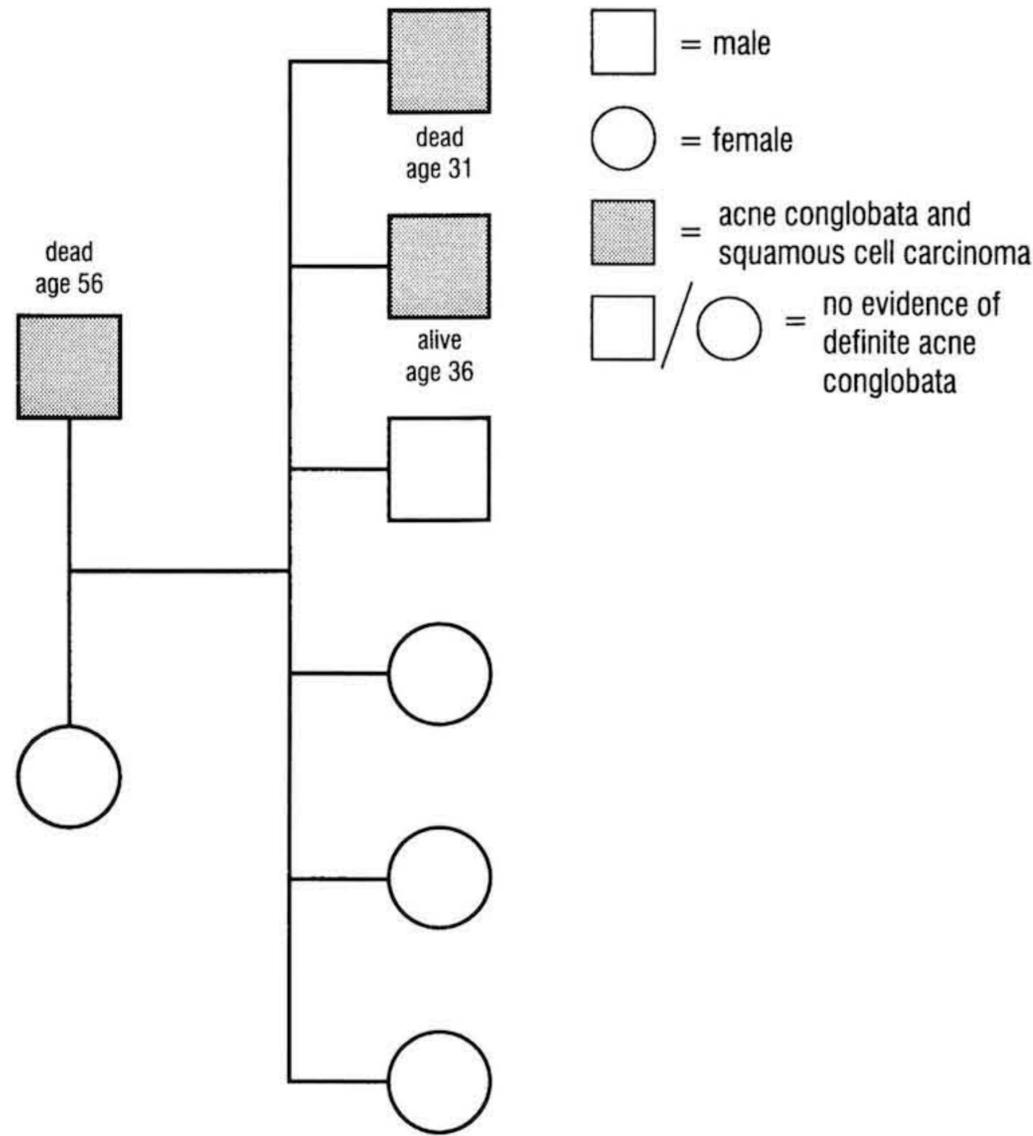


Fig. 5. Family tree.

transmission with complete penetrance (Fig. 5). The certainty with which one can draw this conclusion has not been previously possible or reported.

This series in one family serves to highlight a few important points when one is confronted with acne conglobata. Development of Marjolin's ulcers is possible in almost any long-standing inflammatory or densely scarred lesion. Thus, it is not surprising that it can occur in acne conglobata. Generally, malignant degeneration has been noted to occur with a latency of 11–50 years³. Genetic co-transmission of acne conglobata and increased susceptibility to squamous cell carcinoma is possible, as evidenced by our patient and his family. The malignant lesions are often noted to be very well differentiated. In fact, they may be so well differentiated as to give rise to the falsely negative biopsies that were, in fact, evident in our patient's sibling initially. The areas where Marjolin's ulcers arise are often

areas with such severe scarring and past, as well as present, inflammation, that malignant degeneration and subsequent infiltration may be quite advanced before obvious detection of tumor is possible. Thus, in this subset of patients, a very high index of suspicion must be maintained. Similarly, if an area appears clinically suspicious for carcinoma, deep biopsies should be repeated and early excisional biopsy contemplated. From our experience, it appears that, although these tumors tend to be exceptionally well differentiated, once established, they run a locally aggressive, unremitting course. Early and aggressive surgical therapy combined with a full course of external beam radiotherapy seems to offer the only hope of cure at this time. Early treatment of patients with acne conglobata with isotretinoin therapy has been shown to be beneficial in controlling their disease progression¹. This therapy should be considered in high risk patients with either a family history of malignant

degeneration and/or a personal history of severe progressive inflammatory acne conglobata. By decreasing the inflammation and subsequent scarring, one cannot only alleviate the often disfiguring skin manifestations of this disease but, perhaps, decrease the possibility of unusual malignant degeneration that is occasionally seen.

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