Multiple Keratoacanthomas Developing After Chronic Azathioprine Exposure: A Case Report

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Received date: 17 November 2022, Manuscript No. DMCR-22-20170; **Editor assigned:** 19 November 2022, Pre QC No. DMCR-22-20170 (PQ); **Reviewed:** 21 November 2022, QC No. DMCR-22-20170 (Q); **Revised:** 24 November 2022, Manuscript No. DMCR-22-20170 (R); **Published date:** 26 November 2022 doi. 2684-124X .2022.7.(3).10004

Abstract

Azathioprine is an immunosuppressive agent that poses an increased risk of developing squamous cell carcinomas to include the self-involuting squamous cell carcinoma variant, a keratoacanthoma. The development of multiple keratoacanthomas is considered rare and there are limited reports in the literature of multiple keratoacanthomas developing in patients after exposure to azathioprine. We present a case of multiple keratoacanthomas developing after 28 years of azathioprine use in a patient without any genetic predisposition.

Keywords: Case report • Azathioprine • Keratoacanthoma

Introduction

Azathioprine is a widely prescribed immunosuppressant, which confers its immunosuppression by converting into several metabolites that inhibit cell synthesis. One of the metabolites, 6-thioguanine, is hypothesized to increase the risk of keratinocyte carcinomas via DNA oxidation upon UVA exposure [1]. Self-healing squamous cell carcinoma (SCC), or keratoacanthoma (KA), is among those that develop at an increased rate [2,3]. To date, there have been limited cases in the literature reporting multiple KAs associated with azathioprine. We report a case of multiple KAs developing in a patient receiving long-term azathioprine therapy.

Case History

A 55 year-old Caucasian female with autoimmune hepatitis was treated with azathioprine for 28 years and reported no personal or family history of skin cancer. She presented to the dermatology clinic with several years of recurrent eruptions of painful, scaly, volcano-like papules that spontaneously involuted into macular scarring over her trunk and extremities. On examination, several hypopigmented macules (Figure 1A) were observed throughout the body at prior self-involuted lesion sites. There was also a 4 mm brown and yellow scaly volcano-like papule on the right thigh that persisted for over two years (Figure 1B). A shave biopsy of this papule showed a KA type squamous cell carcinoma. As the initial biopsy transected the lesion at the base, a deeper biopsy was performed that revealed biopsy site changes without evidence of residual SCC. Biopsy of one of the many hypopigmented macules at sites of prior similar appearing scaly volcano-like papules confirmed only residual scar tissue. As a result, the patient was clinically diagnosed (Figure 2) with multiple KAs and followed closely with full body skin exams [4].

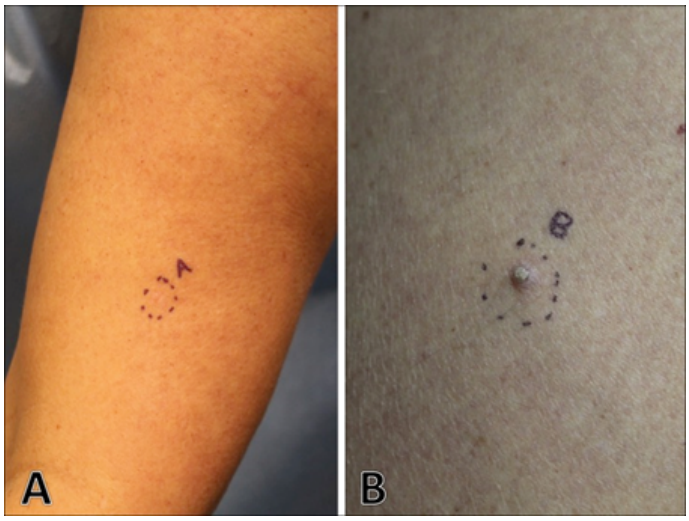

Figure 1(A,B). Different stages of keratoacanthoma. A. One of the macular scarrings as a result of previously self-involuted keratoacanthoma. B. A brown and yellow scaly volcano-like papule on the right thigh that persisted for 2 years.

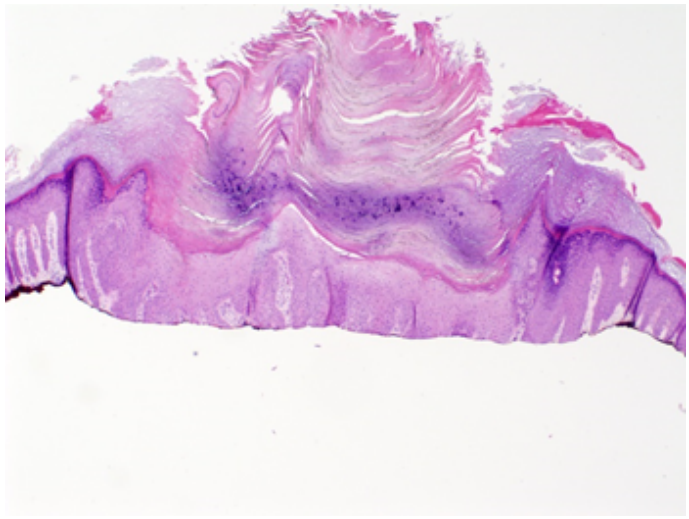

Figure 2. Histopathology shows the silhouette of a buttressed endo-exophytic squamous neoplasm. Keratinocytes within the neoplasm demonstrate enlarged glassy cytoplasms and there is thick overlying hyper-parakeratosis. The findings are those of a keratoacanthoma type squamous cell carcinoma.

Discussion and Conclusion

Multiple KAs can present as familial Ferguson-Smith (FS) or Grzybowski type (GEKA). FS is an autosomal dominant disorder with a 3:1 male predominance that begins in the second decade of life4. KAs usually appear in sun-exposed areas ranging from a few to a hundred rapidly growing 2cm-3cm nodules [5]. GEKA has similar prevalence among genders. It occurs in the fifth to seventh decades and presents with hundreds to thousands of 1mm-2mm follicular papules [3, 6]. In our case, the patient's clinical presentation does not resemble familial multiple KAs. Although the precise etiology of azathioprine induced keratinocyte carcinomas is unclear, azathioprine poses a 56% increased risk of SCC compare to other immuno-suppressants [2]. Therefore, high clinical suspicion for multiple KAs and vigilance during routine screening to rule out malignant transformation in patients exposed to azathioprine remain the best early intervention.

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Cite this article: Zhang, SX et al. Multiple Keratoacanthomas Developing After Chronic Azathioprine Exposure: A Case Report 2022, 7(3), 001-01-02.