CASE REPORT

Quinacrine: An Effective Addition to the Treatment of Refractory Cutaneous Lupus Erythematosus

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Summary

Treatment of refractory cutaneous lupus is challenging. When conventional therapy, including hydroxychloroquine (HCQ), corticosteroids and immunosuppressants, has failed, the addition of quinacrine may be a promising option. We describe a case of refractory chronic cutaneous lupus erythematosus (CCLE) who responded well to quinacrine.

Key words: *Quinacrine, Refractory cutaneous lupus erythematosus, Hydroxychloroquine*

Introduction

Quinacrine, also known as mepacrine, is a synthetic quinine derivative which has been shown to be efficacious in the treatment of discoid lupus erythematosus (DLE) as early as in the 1940s.[1-3] However, its use was superseded by hydroxychloroquine (HCQ) because of quinacrine's purported side effects. Nevertheless, the use of quinacrine has seen a resurgence of late. We report a case of refractory chronic cutaneous lupus erythematosus (CCLE) who responded favourably to quinacrine.

Case Report

Our patient is a 49-year-old man who was diagnosed with systemic lupus erythematosus 22 years ago based on the American College of Rheumatology (ACR) 1997 revised classification criteria for SLE.[4] He is anti-nuclear antibody positive but anti-double-stranded DNA and extractable nuclear antigen negative. His complement levels (C3/C4) were never low. He had mild cytopenias (leukopenia and lymphopenia) in the past but no major organ involvement. His manifestations are predominantly cutaneous: he has disfiguring DLE rashes on the scalp, face and both upper arms and forearms.

His rashes (Figure 1a) are refractory to almost all immunosuppressants that he has tried: multiple rounds of intravenous immunoglobulin and IV methylprednisolone, cyclosporine, azathioprine, colchicine, dapsone, methotrexate and mycophenolate mofetil. These were all used

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on a background of HCQ and topical and systemic corticosteroids. He is steroid-dependent, often flaring when his prednisolone dose is reduced to less than 20mg daily. He is on HCQ 400mg daily, the maximum recommended dose. He developed avascular necrosis of both femoral heads and recurrent serious infections as a result of prolonged high-dose corticosteroid use.

He is an ex-smoker who stopped in 2018 because of the development of peripheral vascular disease and ischemic heart disease. However, despite stopping smoking, his rashes remained active. In late 2019, we applied for special permission to purchase and use quinacrine through the Ministry of Health, as it is not licensed for use in Malaysia. Quinacrine 100mg daily was added to HCQ and prednisolone. He reported progressive improvements in his rashes in the first 6 months. CLASI activity scoring improved from 15 to 2. His prednisolone dose was reduced gradually to 5mg daily. He has now been on quinacrine for 15 months: his lesions have remained inactive and his prednisolone use has not required dose escalation. He has not developed any untoward side effects to quinacrine. Figure 1b shows his cutaneous lesions 6 months after initiation of quinacrine.

Figure 1. Side profile of the patient's face showing DLE rashes; (a) Pre-treatment; (b) Post

Discussion

Antimalarials, together with non-pharmacological methods like smoking cessation and sunscreen usage, are recommended as first-line treatment for cutaneous lupus erythematosus (CLE). Quinacrine is added when there is poor response, where quinacrine has been shown to work synergistically with HCQ or chloroquine.[5]

Antimalarials have been used to treat CLE for years but their mechanism of action is not completely understood. Recent studies have implicated toll-like receptors (TLRs) in the pathogenesis of CLE in producing pro-inflammatory cytokines like interferon-α (IFN-α).[6-7] Antimalarials are able to inhibit TLRs, hence dampening production of IFN-α.[8] Quinacrine and HCQ were shown in a study to decrease the production of IFN-α.[9] Other postulated mechanisms of action of antimalarials include immunomodulatory, anti-proliferative, anti-inflammatory and photoprotective properties.[10]

Quinacrine is a safe drug with relatively few side effects. Notably, it has no retinal toxicity[11-12] and does not potentiate the side-effects of HCQ or CQ when used in combination.[13] However, the commonest side effect is a yellowish discolouration of the skin, which reverses upon cessation of the drug. Other side effects which could occur include headache and gastrointestinal symptoms.[13] Rare side effects include aplastic anaemia[14] and acute hepatitis,[15] although these occurred in conjunction with the use of other drugs and concomitant Hepatitis C infection.

Quinacrine appears to be more efficacious in patients with acute cutaneous lupus and discoid lupus, with response rates ranging from 55-80%.[15-18] However, it is still not widely available in the United States of America, Europe or Asia.[11,17,19] thus limiting its use. Nonetheless, we hope this experience would encourage the use of quinacrine in refractory cutaneous lupus in Malaysia and help reduce the incidence of adverse effects with other immunosuppressants.

Conclusion

Several case series have supported quinacrine's efficacy and safety. It can be considered in patients with DLE who do not show adequate response despite maximal HCQ therapy and corticosteroid therapy.

Conflict of Interest Declaration

The authors have no conflict of interest to declare.

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