Mycophenolate Mofetil in Refractory Cutaneous Lupus Erythematosus: No Definitive Evidence

To the Editor:

We read with great interest the article by Tselios, *et al* on mycophenolate mofetil (MMF) in nonrenal manifestations of systemic lupus erythematosus (SLE)[1]. The study suggested that this treatment is an efficacious alternative in refractory to standard-of-care of nonrenal manifestations of SLE in the long term[1]. However, some data are lacking to change our clinical practice. For instance, with regard to cutaneous lupus erythematosus (CLE) lesions, an improvement was observed at 6 and 12 months in 25.9% and 40.7% of patients without renal involvement, respectively, and at 6 and 12 months in 33.3% and 53.3% of patients with renal involvement, respectively[1]. Such a result is very interesting in our daily practice because of conflicting data in the literature, as indicated by the authors. However, we have a few comments on this article about the definition of CLE, the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) used to assess the severity of skin lesions, and the response under MMF and concomitant treatment with antimalarial agents in this cohort.

First, a better definition of skin lesions should have been necessary in the study since a wide range of specific lesions of lupus erythematosus were identified. The authors indicated that patients had acute CLE, but no other subtypes of CLE were reported. Of note, specific skin lesions of lupus erythematosus are currently classified into 4 different categories[2]. Acute CLE includes, for instance, localized forms with the classic "malar rash" and erosions and ulcerations of the oral mucosa, and less common generalized forms. Subacute CLE consists of symmetric erythematous macules and papules turning into papulosquamous and psoriasiform lesions with a frequent annular and polycyclic form on sun-exposed areas. Chronic CLE includes discoid lupus, lupus erythematosus profundus, and chilblain lupus erythematosus. Finally, intermittent CLE or lupus erythematosus tumidus is characterized by indurated urticarial-like single or multiple plaques on sun-exposed areas. Treatment of CLE can be different depending on the subtype, but always in association with photoprotection.

Then the SLEDAI-2K score consists of 24 items covering 9 organ systems (6 clinical and 3 laboratory) ranging from 0 to 105. It is widely validated in clinical practice, taking into account rash (inflammatory type rash), mucosal ulcers (oral or nasal ulcerations), and alopecia (abnormal, patchy, or diffuse loss of hair)[3]. However, it does not include severity within an organ system and it is not useful for judging activity of the different subtypes of CLE. Other scores are available, such as the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) assessing activity and damage of CLE with inaccurate assessment of the severity of all disease subtypes[4]. Therefore, the Revised CLASI (RCLASI) was proposed, scoring the activity and damage, taking into account the anatomical region (face, chest, arms) and morphological aspects (erythema, scaling/hyperkeratosis, edema/infiltration, scarring/atrophy) of skin lesions[5]. Currently, RCLASI has been shown to be a validated scoring system and has been applied in several clinical trials. It should have been used in Tselios, *et al*'s study to evaluate the efficacy of MMF on CLE.

Finally, hydroxychloroquine (HCQ) is the cornerstone of SLE treatment and the first-line treatment of most of CLE. In daily practice, the monitoring of whole-blood concentration measurement is required because concentration higher than 755 ng/ml was shown to be effective on skin lesions and to prevent lupus flares with a well-known risk of retinal toxicity[5]. Therefore, we were surprised to note that only 80% of patients were taking antimalarials, including HCQ and chloroquine[1]. Moreover, in a recent study including 276 patients with SLE, total noncompliance was observed in 11% of patients and subtherapeutic dosage was recorded in 77% of patients[6]. Further, another study demonstrated that increasing the dosage of HCQ according to blood concentration resulted in 81% of patients (26/32) with refractory CLE[7].

The study by Tselios, *et al*[1] suggests that MMF is effective in nonrenal manifestations of SLE, but further studies including a multidisciplinary panel of experts are required to validate these results. Antimalarials, topical steroids, and calcineurin inhibitors will continue to be the standard of medical care, and thalidomide and analog retinoids and dapsone will continue to be the drugs for refractory CLE.

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