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Belimumab reduces antiphospholipid antibodies in SLE patients independently of hydroxychloroquine treatment

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Antiphosholipid antibodies (aPL) are a well known risk factor for cardiovascular disease and accelerated atherosclerosis in Systemic Lupus Erythematosus (SLE) patients, [1] even in the absence of an overt associated antiphospholipid antibodies syndrome (APS). Moreover, carriers of isolated aPL (especially when at high-titer and triple positivity), have an increased subclinical atherosclerosis, comparable to APS patients [2].

How to prevent cardiovascular manifestations in SLE patients with aPL is still a matter of debate.

Low dose aspirin and hydroxycloroquine (HCQ) have a role as primary prophylaxis [1]. In particular, HCQ seems able to significantly reduce aPL in APS patients [3].

Recently, Sciascia et al. reported the disappearance of aPL in three patients with SLE-associated APS treated with belimumab, with subsequent re-positivation of aPL following treatment discontinuation [4]. However, as stated by the Authors, a role of HCQ in this reduction cannot be excluded.

Herein, we report the outcome of 12 SLE patients (10 females, median age 45, range 39–56) with aPL positivity, treated with belimumab for a median of 13 (6.5–38) months. Seven patients also met the criteria for the diagnosis of APS (6 for thrombotic events and 1 for obstetric complications), whereas five were aPL carriers. All the patients had persistent aPL positivity confirmed as previously described [4]. Of the twelve patients, three had never been on HCQ, four were already on HCQ before starting belimumab and continued it throughout treatment. Two patients discontinued and three patients started HCQ during belimumab treatment.

Patients already treated with HCQ before belimumab had considerably lower baseline aCL levels as compared to those not treated. Nevertheless, a significant reduction in aCL occurred in both groups following belimumab treatment. In patients never treated with HCQ, aCL decreased from 67.5 (7.1–179) to 14.3 (2.8–83) ($\Delta = -49.2$ (-96; -4.3); $p = .028$), whereas in patients always treated with HCQ, aCL decreased from 15 (4.4–45.5) to 2.25 (1–9.2) ($\Delta = -11.35$ (-31; -3.4); $p = .017$) (Fig. 1). In detail, in patients never treated with HCQ, aCL-IgG decreased from 232.5 (123–342) to 136.5 (23–250) and aCL-IgM decreased from 95.5 (12–179) to 44.3 (5.6–83). In patients consistently treated with HCQ, aCL-IgG decreased from 35 (11–208) to 2.6 (1.9–13) and aCL-IgM decreased from 37.5 (19–56) to 10.7 (5.4–16).

Moreover, as reported for aCL, patients already treated with HCQ before starting belimumab had considerably lower baseline levels of antiβ2 GPI as compared to those not treated. Following belimumab administration, a reduction of antiβ2 GPI occurred, both in patients never or consistently treated with HCQ (from 60.5 (1.3–136) to 25.5 (0.4–112), and from 2.25 (1.65–11) to 1.8 (1.05–4.2), respectively), although statistical significance was only found for patients not treated with HCQ ($\Delta = -2$ (-69; -0.9); $p = .035$). (Fig. 1).

Of note, in both groups no atherothrombotic events occurred during belimumab treatment. The retrospective nature of our study, and the small number of reported patients, are certainly the main limitations of our study. Nonetheless, we report for the first time the ability of belimumab to reduce aPL independently of concomitant HCQ in SLE patients. Despite usually safe, systemic and skin reactions and ocular toxicity have been described in patients treated with HCQ, prompting its discontinuation [5]. In this setting, a different drug able to reduce aPL may be essential. Interestingly, in our cohort, patients already on HCQ showed a progressive reduction of aPL also after belimumab treatment, suggesting an additional beneficial effect of the biologic drug.

Prospective controlled studies on a larger population are needed, not only to confirm these findings, but also to evaluate the clinical significance of aPL reduction in terms of prevention of atherothrombotic events.

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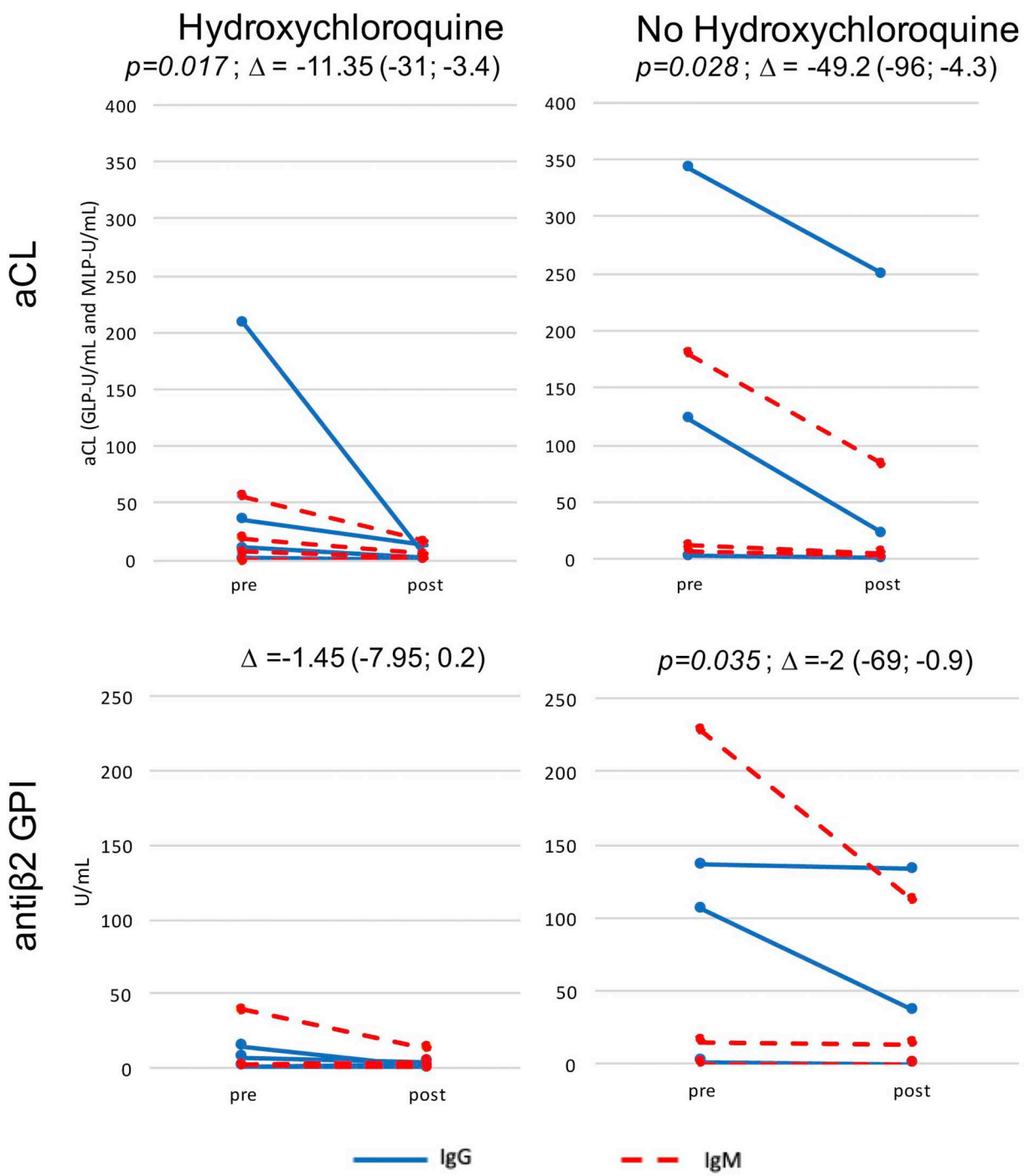

Fig. 1. Variations in the levels of anti-cardiolipin (aCL) and anti-beta2 glycoprotein I (antiβ2 GPI) IgG and IgM antibodies, before vs after treatment with belimumab in patients treated or never treated with hydroxychloroquine.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.autrev.2018.11.002.

References

[1] Pons-Estel GJ, Andreoli L, Scanzi F, et al. The antiphospholipid syndrome in patients with systemic lupus erythematosus. J Autoimmun 2017;76:10–20.

[2] Di Minno MND, Emmi G, Ambrosino P, et al. Subclinical atherosclerosis in asymptomatic carriers of persistent antiphospholipid antibodies positivity: a cross-sectional study. Int J Cardiol 2018. https://doi.org/10.1016/j.ijcard.2018.06.010. article in press.

[3] Nuri E, Taraborelli M, Andreoli L, et al. Long-term use of hydroxychloroquine reduces antiphospholipid antibodies levels in patients with primary antiphospholipid syndrome. Immunol Res 2017;65:17–24.

[4] Sciascia S, Rubini E, Radin M, et al. Anticardiolipin and anti-beta 2 glycoprotein-I antibodies disappearance in patients with systemic lupus erythematosus and antiphospholipid syndrome while on belimumab. Ann Rheum 2018. https://doi.org/10.1136/annrheumdis-2018-213496.

[5] Costedoat-Chalumeau N, Dunogué B, Leroux G, et al. A critical review of the effects of hydroxychloroquine and chloroquine on the eye. Clin Rev Allergy Immunol 2015;49:317–26.

Giacomo Emmi[a,*,1], Alessandra Bettiol[a,b,1], Boaz Palterer[a], Elena Silvestri[a], Gianfranco Vitiello[a], Paola Parronchi[a], Domenico Prisco[a]

[a] *Department of Experimental and Clinical Medicine, University of Firenze, Italy*

[b] *Department of Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA), University of Firenze, Italy*

E-mail address: giacomaci@yahoo.it (G. Emmi).

[*] Corresponding author at: Department of Experimental and Clinical Medicine, University of Firenze, Italy Largo Brambilla 3., 50134 Firenze, Italy.

[1] These Authors equally contributed.