opment, would have been welcome to complete this excellent review.

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Reply

To the Editor:

We thank Dr. Vuilleumier for his interest in our review of HDLs in SLE and his comments on anti–Apo A-I autoantibodies. Dr. Vuilleumier raises an important point, with which we fully agree, that the prevalence of increased levels of anti–Apo A-I is not specific to SLE. The frequency of positivity for these antibodies in different diseases is summarized in Table 1. Inconsistent results could be attributed to between-assay differences introduced by the use of different enzyme-linked immunosorbent assays (ELISAs) and different cutoff values used to assess positivity (1).

Questions were also raised concerning whether anti–Apo A-I is an independent predictor of cardiovascular events in SLE patients. Indeed, it has not been found to be independently associated with cardiovascular events in SLE (2,3) though, as pointed out by Dr. Vuilleumier, an association between anti–Apo A-I and cardiovascular events has been demonstrated in a broad array of other clinical settings (4). This inconsistency certainly warrants further investigation.

Dr. Vuilleumier also raised questions about our hypothesis that oxidized Apo A-I may play a role in inducing anti–Apo A-I autoantibodies. We acknowledge that the formation of anti–Apo A-I autoantibodies could be attributed to various genetic and environmental factors, as he notes. At the same time, our hypothesis is based on our experience in the biopharmaceutical field, where oxidation and misfolding are recognized immunogenic factors for therapeutic proteins and peptides (5,6). In the case of Apo A-I, oxidation at Met-112 and Met-148 has been suggested to cause conformational change of Apo A-I by disrupting the α-helix structure (7,8). Methionine oxidation on Apo A-I has also been shown to induce the formation of amyloid fibril, which could be immunogenic (9). Studies by Henson and Venditto showed that Apo A-I peptide with oxidized Met-148 could bind with goat polyclonal antibodies against human Apo A-1 (10), and oxidized Apo A-I appeared to be more immunogenic in mouse models (11). In addition to methionine oxidation, Apo A-I could undergo other oxidative modifications, such as with 3-chlorotyrosine and 3-nitrotyrosine in autoimmune settings (12,13). Particularly, 3-nitrotyrosine modification has been proven to be immunogenic for other proteins and was suggested to be responsible for impaired immunologic tolerance (14). Thus, further studies on 3-chlorotyrosine– and 3-nitrotyrosine–modified Apo A-I would be helpful to inves-

Table 1. Prevalence of anti–Apo A-I autoantibodies in different populations*

Author, year (ref.)	Population	Prevalence, %	Positivity cutoff
Antiochos et al, 2017 (15)	5,220 participants from the general population (mean age 52.6 years)	19.9	97.5% of the reference distribution from 140 healthy blood donors
Satta et al, 2018 (16)	237 HIV patients with no current lipid-lowering therapy	58	97.5% of the reference distribution from 140 healthy blood donors
Pruijm et al, 2012 (17)	71 patients receiving maintenance hemodialysis	20	97.5% of the reference distribution from healthy blood donors
Vuilleumier et al, 2010 (18)	69 RA patients, 46 matched controls	17 in RA patients; 2 in healthy controls	97.5% of the reference distribution from healthy blood donors
Nigolian et al, 2020 (3)	76 patients meeting EULAR/ACR criteria for SLE (19)	43	97.5% of the reference distribution from 48 healthy donors
Butuca et al, 2007 (20)	55 SLE patients, 150 age- and sex-matched healthy controls	36 in SLE patients; 0.7 in healthy controls	>5 SD above the mean in healthy controls
O'Neill et al, 2010 (21)	39 SLE patients with high disease activity, 42 SLE patients with low disease activity, 34 healthy controls	35.9 in SLE patients with high activity; 12 in SLE patients with low activity	>3 SD above the mean in healthy controls
El-Lebedy et al, 2016 (22)	102 patients with type 2 DM, 112 patients with type 2 DM and CVD, 88 healthy controls	8.8 in patients with type 2 DM; 35.7 in patients with both type 2 DM and CVD; 6.1 in healthy controls	Absorbance ≥2.1 OD using human anti–apolipoprotein AI antibody ELISA kit (#MBS7034; MyBioSource)

* Anti–Apo A-I = anti–aolipoprotein A-I; RA = rheumatoid arthritis; EULAR = European League Against Rheumatism; ACR = American College of Rheumatology; SLE = systemic lupus erythematosus; DM = diabetes mellitus; CVD = cardiovascular disease; ELISA = enzyme-linked immunosorbent assay.

tigate the underlying mechanisms of anti–Apo A-I autoantibodies in autoimmune settings.

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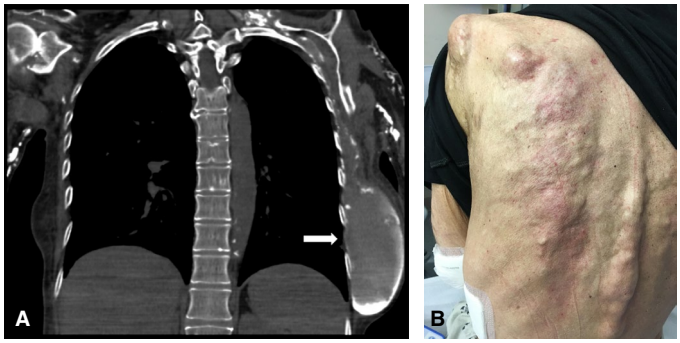
Clinical Images: Giant calcinosis in dermatomyositis and scleroderma overlap



The patient, a 56-year-old woman with a history of dermatomyositis and scleroderma overlap with positive PM/Scl-75, was admitted with a severe myopathy flare. The disease had been characterized by Raynaud's phenomenon, extensive calcinosis cutis, mild interstitial lung disease, elevated creatine kinase level, and proximal muscle weakness. Previous treatment with methotrexate had been discontinued 6 months prior, due to a severely infected area of calcinosis with a subsequent septic arm. Monthly intravenous immunoglobulin (IVIG) and low-dose prednisone were continued. Three months after finishing antibiotic treatment, the patient presented with severe dysphagia, dyspnea, Gottron's papules, and weakness. Interestingly, a new lump in the posterior aspect of the left flank had been growing progressively. Computed tomography of the chest showed a lobulated, heterogeneous fluid collection (9.8 × 5.6 × 16.5 cm) (**arrow** in **A**) within the subcutaneous soft tissue of the left lateral chest wall and extensive calcinoses covering the margins and in isolated pouches. Needle aspiration yielded 1 ml of white, dense matter suggestive of calcinosis. A drainage tub was surgically inserted for a week, emptying the collection. Cultures were negative. After 2 weeks, a stable, minimal amount of fluid (2 × 2 × 4 cm) reappeared (**B**). Previous calcinoses had been drained in the flexures, and an attempt at injecting intralesional sodium thiosulfate had been unsuccessful. Calcinosis is a common, impairing manifestation of dermatomyositis and scleroderma that can appear unrelated to disease flares. No proven treatments are available. The myositis flare in this patient was treated with methylprednisolone boluses, IVIG, and intravenous cyclosporine and gradually improved.

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