are within the range reported in the general population." In preparing the final proofs, the text was changed to "In the current study, the frequency of headache at the enrollment visit *was comparable* to the 1-year prevalence rates reported by Stovner and Andree in the general population, as the study enrollment window captured all headaches that were reported 6 months prior to diagnosis of SLE up to enrollment, which occurred a mean 5.6 months following the diagnosis of SLE."

Furthermore, the sentence that followed this and which was complementary to the previous sentence was split from the preceding text and started as a new paragraph in the proofs. Regrettably, these editorial changes were not flagged with an "author query" when the proofs were provided for review.

As Dr. Liebling acknowledges, the format of our Table 1 was constructed to indicate that information on autoantibodies was not available on all patients at the enrollment visit. Our extensive analysis did not reveal any association between headache and autoantibodies, which is what was reported in the article. The questions posed by Dr. Liebling are centered on potential "informative missingness." As acknowledged in the Discussion, a limitation of our study was the fact that autoantibodies were measured only at the enrollment visit. It is possible that had this information been available on all patients at enrollment a clinical–serologic association may have emerged, but this is speculative, and we can only work with the data that were available. Finally, some of the headache subsets (e.g., "lupus headache" and others) contained too few patients to permit robust statistical analysis.

The nature of our study design does not provide data to enable determination of the reasons for resolution of different headaches, especially those that were infrequent, including "lupus headache" and intractable headache. Furthermore, a substantial portion of the Discussion is devoted to the need to better define the controversial issue of "lupus headache."

We do not agree with Dr. Liebling that there was an apparent discordance between our decision models (for determining attribution of neuropsychiatric events) and one of the stated objectives of the study (i.e., "to address the discrepant findings and conclusions in the literature"). The decision attribution models for neuropsychiatric events have been used in a consistent manner in multiple studies of neuropsychiatric disease in the Systemic Lupus International Collaborating Clinics inception cohort since 2007. Dr. Liebling is correct that these attribution models exclude SLE as the cause all headaches. In the report we stated explicitly "A priori, these decision rules excluded SLE as the cause of all headaches identified within the cohort." We also pointed out that headache could occur in SLE patients "as one component of a broader NPSLE event (e.g. meningitis, seizure, cerebrovascular disease)" and that "there is a need to better define isolated lupus headache and to reach consensus on whether it is truly a stand-alone manifestation of NPSLE." In short, the overall objective of our study was to examine *all* headaches in our cohort and provide new information on an area of controversy and clinical need in SLE. In so doing we have reported "the frequency, characteristics, associations with clinical variables and autoantibodies, and impact of [all] headache[s] on health-related quality of life in a large, prospective, multiethnic, international inception cohort of SLE patients".

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The beneficial effect of abatacept in lupus nephritis may include stabilization of β1 integrin activation in podocytes and Treg cell repopulation: comment on the article by Furie et al

To the Editor:

We read with great interest the recent article by Furie et al (1) in which they described the first randomized, placebo-controlled trial of the efficacy and safety of intravenous abatacept (a CTLA-4Ig fusion protein), when used on a background of mycophenolate mofetil and glucocorticoids, in adult patients with lupus nephritis. The results of that study showed improved levels of anti–double-stranded DNA (anti-dsDNA) antibodies, complement, and urinary protein (1). According to the authors, the rationale for considering abatacept for the treatment of lupus nephritis included "not only preclinical evidence that CTLA-4Ig is effective in treating and preventing nephritis in the NZB × NZW mouse model . . . but also observations in a study of extrarenal lupus indicating favorable effects on anti-dsDNA antibody levels."

We would like to propose another beneficial mechanism of abatacept in lupus nephritis. Abatacept is a costimulatory inhibitor that targets B7-1 (CD80) (2), and podocyte expression of B7-1 has been shown to be correlated with the severity of human lupus nephritis (3). A recent study showed that abatacept might stabilize β1 integrin activation in podocytes and reduce proteinuria in patients with B7-1–positive glomerular disease (4).

Although the exact etiology of lupus nephritis remains elusive, a depletion of the natural Treg cell subpopulation has been implicated in the pathogenesis of this disease (5). Notably, Wei et al showed that FoxP3-positive Treg cells were up-regulated significantly by CTLA-4Ig treatment (6).

Therefore, abatacept might also have a beneficial effect in lupus nephritis by stabilizing β1 integrin activation in podocytes and inducing Treg cells, in addition to reducing anti-dsDNA antibody levels. Further studies are necessary to evaluate populations of Treg cells and changes in β1 integrin activation in podocytes before and after abatacept treatment in lupus nephritis.

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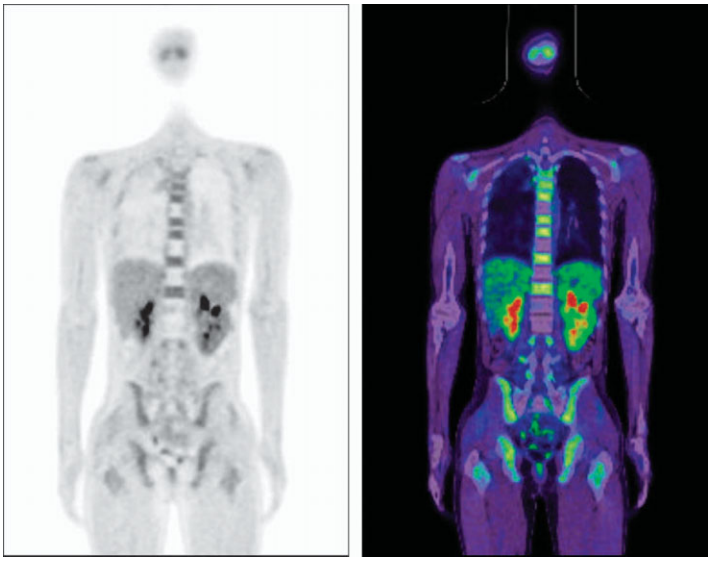
Clinical Images: Multiple osteonecrotic lesions mimicking a piano keyboard in the spine of a patient with catastrophic antiphospholipid syndrome



The patient, a 15-year old boy, was referred to the clinic because of seizure activity and unexplained fever. A comprehensive diagnostic workup revealed extensive thrombosis in the brain, lung, kidney, and spleen. Antiphospholipid antibodies were positive at high titers, without other serologic evidence of combined autoimmune diseases. A diagnosis of catastrophic antiphospholipid syndrome (APS) was made, and anticoagulation therapy was started. Positron emission tomography, which was performed to evaluate hidden malignancies, showed a pattern of alternating photon defects at the vertebrae, mimicking the black and white keys on a piano keyboard. When vertebral malignancy is treated with radiotherapy, this pattern is known to appear. In an effort to rule out cancer, a multidisciplinary approach that included other imaging studies and laboratory tests was used and revealed no evidence of malignancies. Based on the patient's clinical manifestations, the "cold" vertebrae were considered to represent multifocal osteonecrosis of spine, which was managed with conservative treatment. Osteonecrosis, also called avascular necrosis of bone, is defined as death of bone caused by obstruction of the blood supply. A prothrombotic state characteristic of APS can be one of the risk factors for osteonecrosis. Several such cases have been reported in association with APS, especially catastrophic APS (1–3). The diagnosis depends mostly on the imaging modalities used, and a nonsurgical therapeutic approach is preferred in cases of asymptomatic disease (3).

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