RDS comments on Virtual Grand Rounds in Dermatology Case for David Elpern - July 7, 2011 "I am a monster" case of SCLE/CCLE

Diagnosis

I suspect that this woman's initial diagnosis was SCLE but due to the therapeutic refractoriness and persistence of her SCLE disease activity she has evolved superficial cutaneous atrophy in her lesions evident on the photographs that could raise the question of classification currently as generalized discoid LE (we have seen and informally published such transitions in prior chapters and reviews that we have written in the past). However, her elevated Ro/SS-A autoantibody levels and her low complement levels would argue in favor of SCLE over generalized DLE. In addition, her refractory joint symptoms and elevated rheumatoid factor level would raise the possibility of an overlap with rheumatoid arthritis (ie, "Rupus"). SCLE has been more often reported to overlap with rheumatoid arthritis that has discoid LE. Also, this is the type of patient who can develop overlapping features with Sjogren's syndrome over time. Does she have a history of dry eyes or dry mouth? In addition, as David has indicated, her history of a stroke would raise the possibility that she has a procoagulant state resulting from elevated levels of antiphospholipid antibodies. In my experience, the presence of an antiphospholipid antibody-mediated procoagulant state would be more consistent with autoimmune background of SCLE that discoid LE

Biopsies

I agree that her biopsies are consistent with SCLE having some overlapping features of discoid LE due to the treatment refractoriness and long-term persistence of her cutaneous LE inflammation.

Lab results

Were both her C3 and C4 levels low? When SCLE without clinically significant SLE disease activity occurs in the context of either complete or partial genetic complement component deficiency, it is usually either C2 deficiency or C4 deficiency. It has been my personal experience that SCLE occurring in the context of either C2 or C4 genetic deficiency have been more difficult to control medically.

Further Workup

I agree that this patient should be evaluated for the presence of significant elevations of antiphospholipid antibodies. To address this, I would order IgG, IgA, and IgM cardiolipin antibodies, lupus anticoagulant, and antibodies to beta (2) glycoprotein I. If those were

all negative I would next consider screening her for autoantibodies to phosphatidyethanolamine. Such assays are typically available in reference labs.

I would check her thiopurine methyltransferase enzyme blood levels before starting azathioprine to assess her relative risk for severe hepatic and bone marrow toxicity from this drug and guide optimal dosing.

Management

The patient should be strongly encouraged to stop cigarette smoking. There is now good evidence that cigarette smoking is associated with more therapeutically-refractory forms of cutaneous LE. Data now exist suggesting that the metabolic effects of cigarette smoking do not alter antimalarial metabolism or blood levels. It is thus likely that one or more of the numerous noxious chemicals present in cigarette smoke directly contribute to activating (syn. Koebnerizing) the cutaneous LE process. I have had such patients not be able to stop smoking until they tried the combination of Chantix and group support therapy. However, as we know there are potential clinically-significant psychiatric and cardiovascular side effects of Chantix.

Since her skin disease activity appears to have been quite resistant to antimalarial monotherapy with hydroxychloroquine in the past, perhaps thought might be given to restarting the hydroxychloroquine and adding compounded quinacrine 100 mg per day to the hydroxychloroquine for an additive or synergistic antimalarial clinical effect.

In the past, rather than starting a systemic immunosuppressive agent such as azathioprine in a case like this I would first try thalidomide. Beyond antimalarials, thalidomide is probably the most efficacious drug available in controlling LE-specific skin disease activity plus thalidomide is not significantly immunosuppressive. However, the current market cost of thalidomide is approximately $100,000 per year with the price having been driven through the roof because of its newer cancer indication for myeloma. Recently, most of my patients, even those with insurance, cannot begin to afford even the co-pays for a course of thalidomide. However, the patient in question's history of previous stroke would add a complication to a trial of thalidomide. Thalidomide is now recognized to be capable of producing a procoagulant state as a drug side effect and thus could be risky for a lupus patient who has already had a stroke.

If possible (again because of drug cost), I would first try CellCept before azathioprine as I feel that CellCept is a less toxic drug. CellCept is now recognized by rheumatologists and nephrologists to be as beneficial clinically for lupus nephritis as is cyclophosphamide. If I were using either azathioprine or CellCept in the case such as this, I would start at lower doses and increase the dose cautiously while monitoring for

side effects. I would keep the patient on maximal doses of these drugs for 2-3 months before getting up on them.

Both Celgene and Amgen are currently conducting multicenter clinical trials on completely new drug treatments for antimalarial refractory cutaneous LE including SCLE and discoid LE (the absence of clinically significant internal systemic LE disease activity in the patient in question would make her eligible for such trials). I know that Vicky Werth at University of Pennsylvania in Philadelphia has been involved in these trials. In addition, there might be trial study sites in the Boston area. This might be another option for the patient if she were interested.

Questions

Do you make a distinction between chronic cutaneous lupus and subacute lupus and is important? I have already discussed this issue in the Diagnosis section above.

Psychosocial consequences of living with such a disorder for 30 years? In my opinion, they are profound. Quality of life studies have documented that chronic disfiguring skin disease is second only to renal failure and dialysis in its impact on quality of life (even greater than cancer). In addition there are studies showing that disfiguring cutaneous LE can have a particularly difficult impact on quality of life.