Diabetes mellitus and immunosuppressives

Sir,

Immunosuppressive agents like azathioprine, cyclophosphamide, methotrexate (MTX) or cyclosporine A (CYA) are often used as adjuvants with corticosteroid therapy for patients with chronic dermatological disorders like pemphigus. Such patients may also have diabetes mellitus (DM), which is a relative contraindication for corticosteroid therapy, and may need immunosuppressive therapy. Many dermatologists hesitate to use these agents in patients with diabetes mellitus (DM). I would like to discuss this issue.

Azathioprine (AZA), a synthetic purine analogue is one of the main immunosuppressive drugs used in dermatology. Its immunosuppressive effects are caused by the substitution of naturally occurring purine bases in DNA by its active intracellular metabolite 6-thioguanine in actively dividing cells. AZA is effective in the treatment of autoimmune diseases at doses which don’t cause lymphopenia, leukopenia or bone marrow depression. Although AZA can inhibit T-cell function, patients treated with the standard immunosuppressive doses of AZA generally fail to exhibit significant suppression of cell mediated immunity despite a clinical response to therapy. There is little evidence for any consistent effect of AZA on the normal humoral immune response and often AZA fails to inhibit it. The fact that treatment with AZA is associated with an increased incidence of viral infections but not with an increase in bacterial infections has been taken as evidence against any major inhibition of humoral immunity. Swanson et al found that patients with immunologic diseases don’t become agammaglobulinemic as a result of antimetabolite therapy and that adequate levels of immunoglobulins having the usual spectrum of antiviral and antibacterial activities are maintained. He concluded that when used cautiously AZA does not result in a harmful degree of immunosuppression in patient with immunologic diseases. Sharma et al used AZA in four patients who had both parthenium dermatitis and DM and observed its corticosteroid sparing effect.

Cyclophosphamide (CPA) is the most potent immunosuppressant among the synthetic alkylating agents. Several investigators have reported that there is no change in the relative percentage of circulating B and T cells during CPA induced lymphopenia.

Cyclosporine A (CYA) is a fungal metabolite with potent immunosuppressant effect without significant myelotoxicity. In three large controlled studies, use of CYA was found to be successful in blocking or reducing the cytotoxic process in order to favor beta cell regeneration in patients newly diagnosed with insulin dependent diabetes mellitus (IDDM).

IDDM results from autoimmune beta cell destruction which is thought to be triggered by an infection or environmental stimulus. Bansal et al suggested that lack of adequate insulin levels in DM impairs T lymphocyte activity and the elevated levels of immunoglobulins in DM could be due to subclinical infection. Infections are thought to be due to incompletely defined abnormalities in phagocyte function associated with hyperglycemia, as well as diminished vascularization secondary to long-standing DM. Hyperglycemia probably aids the colonization and growth of a variety of organisms.

In view of the inconsistent effects of immunosuppressive agents on T and B cells, their use in a diabetic patient with optimal glycemic control is justified. The impaired immunity of diabetic patients does not debar them from using these agents. In spite of impaired immunity, diabetic patients have been successfully immunosuppressed by using triple therapy with CYA, AZA and prednisone for renal transplantation for many years. Dermatologists can not afford to ignore these drugs in diabetic patients if they are required, particularly in situations where corticosteroids have to be given for a long duration or...
are contraindicated.

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REFERENCES


Serum sickness like reaction with minocycline

Sir,

Minocycline is a semi-synthetic derivative of tetracycline. It is being increasingly used in the treatment of acne vulgaris as it is more effective than the conventional tetracycline and drug resistance is less likely. Unfortunately, its side effects, albeit rare, are not trivial and include drug induced lupus, autoimmune hepatitis, hypersensitivity syndromes, p-ANCA positive cutaneous polyarteritis nodosa and serum sickness like reaction (SSLR). Minocycline induced SSLR was first reported in 1990.3 We have previously reported SSLR with minocycline and now report another case.

A 19-year-old female presented with gross swelling of the face, significant aggravation of her existing acne, a mild cough and a little difficulty in breathing since 2 days. She also had pain in the smaller joints of the hands as well as some larger joints. All these complaints began 48 hours after starting minocycline (50 mg twice daily) which had been prescribed for her nodulocystic acne. The patient could not remember having taken minocycline earlier or developing any reaction to it.

On examination, she had fever (101°F) and was seriously ill. She had generalized tender lymphadenopathy. Her face was markedly edematous. Routine examination of the blood and urine was within normal limits.

Minocycline was immediately stopped and a systemic steroid started along with oral erythromycin. Her condition rapidly improved within the next 3 days and resolved nearly completely within 10 days. She had amenorrhea for the following 2 months.