WORKSHOP 4: REACTION AND NERVE DAMAGE

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Progress in the past 5 years

Clinical. The use of graded, nylon monofilaments (Weinstein) has been accepted as the best way to monitor nerve function in an accurate and highly reproducible way under field conditions. With serial testing "silent neuropathy" can be identified objectively and treatment instituted promptly. Also serial testing can identify therapeutic responses in silent neuropathy or overt neuritis.

Although much nerve injury occurs as overt neuritis during reactions, silent (asymptomatic) neuropathy is common and may occur either during a reaction or in the absence of any reaction.

In the treatment of reversal reactions, aggressive use of corticosteroid therapy has been found to be reasonably safe under field conditions, and need not be restricted to hospitalized patients. In erythema nodosum leprosum, if thalidomide is not available corticosteroid treatment with clofazimine as adjunctive therapy is valuable. In either reaction for refractory patients the use of cyclosporin A or immunosuppressive antimetabolites has been shown to be effective.

With the use of operating microscopes, surgical decompression procedures are now associated with better results and reduced morbidity, bringing back these operations as a part of established management.

Investigative. Recent studies reaffirm the central role of delayed-type hypersensitivity to antigens of *Mycobacterium leprae* in the immunopathogenesis of reversal reactions. Studies of T-cell infiltrates in nerves and of the cytokines produced, in particular tumor necrosis factor-alpha and IL-1-beta, are elucidating the mechanisms of nerve injury in reversal reactions.

M. leprae may also injure nerves by interference with Schwann cell metabolism, by eliciting antibodies, by stimulating autoantibodies, or by antigenic mimicry, via either antibody or T-cell pathways.

Recommendations

Definitions and terminology. For clarity and comparability a definition of "silent neuropathy" is needed. A single standard name for reversal reactions would make this important problem accessible in Medline and other computer databases. A uniformly used terminology for disability or functional impairment or nerve impairment is needed to establish comparability of clinical and investigative studies.

Clinical. For the early identification and prompt treatment of potentially reversible silent neuropathy or neuritis, standardization of nerve functional assessment and scoring is needed in the parameters of tests used, frequency of use and conditions of use. Once identified, recent onset neuritis or neuropathy should be promptly treated with aggressive use of corticosteroids at an initial dose of 40–60 mg of prednisone or prednisolone daily with a slow taper after 4

weeks with monitoring of function (reduction of daily doses by 5 mg at 2-week intervals) until the level necessary to suppress the reaction is achieved. Treatment for 3–6 months or longer is needed. Exercise caution in patients with hepatitis B, strongyloides or tuberculosis. Rest of the limb is essential, as an example, with the elbow at not less than 110 degrees of extension.

If painful neuritis does not respond promptly to vigorous oral corticosteroid therapy or to parenteral dexamethasone administration, then surgical consultation regarding decompression should be sought before injury is irreversible (ideally within 2–3 weeks of onset), but favorable response to surgery may still occur after prolonged delay.

Following surgery or medical intervention, monitoring of nerve function should be carried out for as long as the patient can be followed.

Further studies. The identification of risk factors for neuritis would abet its early identification and prompt treatment.

Because of its ability to inhibit tumor necrosis factor-alpha, a known neurotoxin, a trial of thalidomide in non-ENL neuritis may be warranted.

Where possible, other methods of nerve assessment should be studied such as laser-Doppler blood flow, electroneuromyography, or electronic vibrometry.

Use of corticosteroids in selected field areas should be monitored so that refined, better recommendations can be made for field use. Studies of other agents are encouraged.

Criteria or tests for the accurate differentiation between relapse and reactions (reversal or ENL) are needed for the increasing number of patients receiving short-term multidrug therapy (MDT).

Continued exploration of the mechanisms of reaction and nerve injury is needed. The devastating type 2 reactions in Latin America are a particularly vexing problem needing further study. Also, immunomodulating agents, such as drugs, mycobacterial components, cytokines or vaccines, should be developed for the treatment and prevention of nerve damage.

Since nerve injury or neuropathy may occur after completion of MDT, monitoring at 3-month intervals is necessary in paucibacillary patients for at least 2 years, and in multibacillary cases for at least 5 years.