LETTER

Myasthenia Gravis: Discontinuation of Long-Term Azathioprine

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In 1985 we reported on 15 patients with generalized myasthenia gravis (MG) in whom immunosuppressive therapy with azathioprine (AZA) was discontinued after patients had gone into stable clinical remission as defined previously [1]; 8 of these patients had a clinical relapse within 1 year. We now give an updated account of these patients and report on another 5 patients treated identically.

In the 8 relapsing patients we started AZA again and added corticosteroids for the first 3 weeks (Fig, A). After a few months (range 4–16) of immunosuppression, 4 of the 8 patients again achieved stable remission and AZA was stopped. Two of these 4 patients relapsed a few months later for a second time and we reinstituted the immunosuppressive treatment, whereas the other two continue in stable remission.

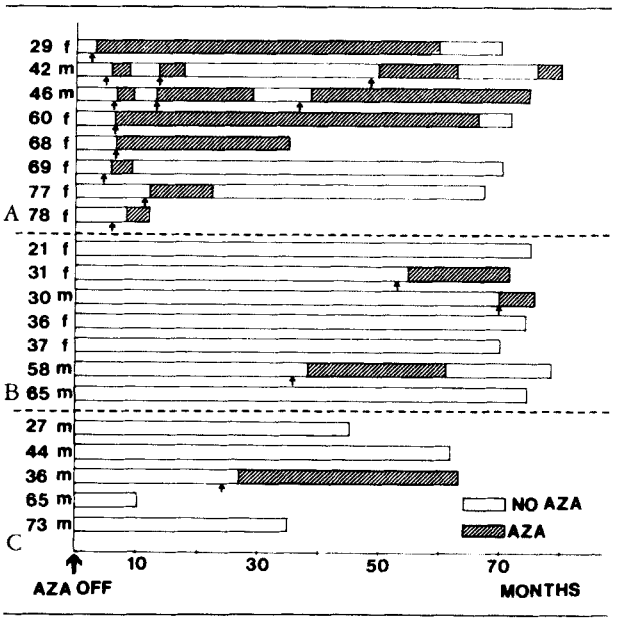
Three of the 8 relapsing patients have had to be maintained on long-term AZA since 1982 for optimal control of symptoms. One of them (29 f) could be taken off AZA and has been without symptoms for 10 months. One patient (78 f) died from a pulmonary embolism 2 weeks after plasma exchange for myasthenic crisis, which had evolved after an initially mild relapse.

In 1 patient (60 f, Fig, A) AZA was discontinued after development of acute renal failure in 1987 following 6 years of therapy with AZA (2.1–2.9 mg/kg). Renal biopsy revealed a primary non-Hodgkin's lymphoma of the kidney. Renal function improved after combined chemotherapy, and the patient's myasthenia remained in remission until she died from adverse reactions to cytostatic drugs [2].

Seven of the original 15 patients had no relapse for a period of at least 38 months after discontinuation of AZA treatment (Fig, B). Later 3 of these 7 patients had a mild clinical relapse and were given a new course of AZA. Before relapse the antibody titer rose twofold in 1 of the 3 patients and slightly in the other 2 patients.

Five additional patients who were not included in the original study [1] were discontinued in stable clinical remission and have been off AZA for 10 to 62 months; only 1 patient relapsed after 26 months (Fig, C). Here the antibody titer rose fourfold at the beginning of the relapse.

In sum, we now follow 20 patients with initially marked generalized MG (Osserman IIb or III, score 0.9 to 3.0 [1]), who went into stable clinical remission while receiving AZA. We reinstituted immunosuppressive drugs only if a clinical relapse occurred and symptoms could not be controlled satisfactorily with pyridostigmine. To date, 12 patients (60%) have developed a relapse after discontinuation of AZA, 8 patients within 3 to 11 months and 4 patients within 27 to 70 months. Four of these 12 relapsing patients gained a new stable remission within 4 to 8 months when treated again and AZA could be discontinued a second time for periods of 8 to 62 months.



Clinical course and azathioprine (AZA) treatment in 20 patients. Before discontinuation of AZA (0 months) all patients had been in clinical remission. Open columns *represent the time without clinical symptoms and without AZA treatment.* Hatched columns *denote a new course of AZA.* Arrows *indicate time of relapse. Age (yr) at time of AZA discontinuation and sex for each patient are given. (A) Patients with relapse; (B) patients without relapse in the earlier report (Fig 1 in [1]); (C) new patients.*

After withdrawal of AZA, close follow-up is essential, with use of autoantibody titer measurements a helpful indicator of the status of the disorder.

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